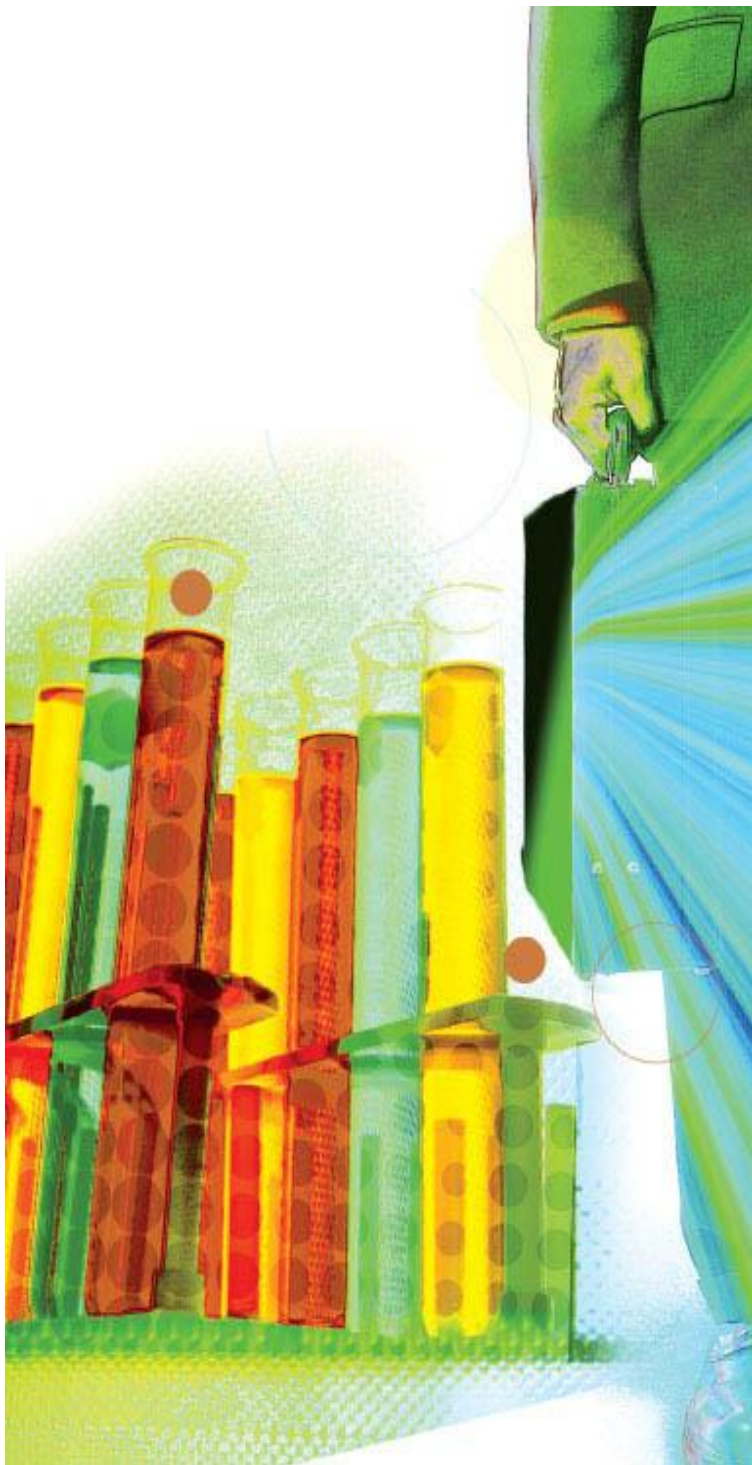


Managing innovations in biotechnology

European Project Semester 2006



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Introduction

The aim of “Managing innovations in biotechnology” is to present the situation, strategies and trends of the innovations management on the biotechnology background. The project is structured in five chapters that intend to offer a comprehensive understanding of the current situation, problems and trends in biotech. At the end, final conclusions are formulated.

The project has been developed by participants from Poland, France, the Netherlands and Spain. Therefore, the analysis has an international perspective, mainly focusing on the above countries.

The theoretical exposition will be contrasted in the last chapters of the project with the real management of a biotech company, with the data and information obtained during a visit to a Polish biotech company.

The project has the following structure:

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Chapter 1

Introducing biotechnology

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Chapter 1

Introducing biotechnology

Introduction

What is biotechnology? What is the history of this amazing life science? Nowadays a huge progress in this domain of technology can be observed. This chapter provides the most relevant facts and figures on the origins of biotech.

What does biotech mean? What are the advantages and disadvantages of biotechnology? Is it possible that this domain will attain the position of the world's leader of technology? Are there many obstacles for this area (ethical issues)? An analysis of all these points is undertaken in the chapter, aiming to offer some clear conclusions.

1.1 Definition: Biotechnology

As exposed further in the project, biotechnology is an enormously wide field of science and technology. It embraces many branches, from techniques to improve crops productivity to the manipulation of human genes. Thus, in an attempt to comprehend all biotechnological activities, the following definition is provided:

A set of biological techniques developed through basic research and now applied to research and produce development¹.

¹ ACGT: Alliance for Cancer Gene Therapy

1.2 Chronology

1919

- The first use of the word *biotechnology*.

1938

- Commercial production of a bio pesticide (*Bacillus thuringiensis*) begins in France

1946

- The U.S. Congress recognized the threat posed by loss of genetic diversity, and provided funds for systematic and extensive plant collection, preservation and introduction.

1953

- The DNA was described as a double helical structure by James Watson and Francis Crick's.

1964

- The International Rice Research Institute in the Philippines starts the Green Revolution with new strains of rice that double the yield of previous strains if given sufficient fertilizer.

1965

- Harris and Watkins successfully fuse mouse and human cells.

1969

- An enzyme is synthesized in vitro for the first time.

1975

- The US Government first urged to develop guidelines for regulating experiments in recombinant DNA: Asilomar Conference, California.

Also in the 1970's

- A first commercial company founded to develop genetically engineered products.

1981

- A mouse first transgenic animal was created.
- Chinese scientist becomes the first to clone a fish: a golden carp.

1983

- The polymerase chain reaction (PCR) technique is conceived. PCR uses heat and enzymes to make unlimited copies of genes and gene fragments.
- The first artificial chromosome is synthesized.

1986

- The U.S. government publishes the *Coordinated Framework for Regulation of Biotechnology*.
- The first field tests of transgenic plants (tobacco) are conducted.

1987

- The first approval for a field test of modified food plants: virus resistant tomatoes.

1988

- A patent for a process to make bleach-resistant protease enzymes to use in detergents is awarded.
- The US Congress funds the Human Genome Project to map the human genetic code.

1990

- Chy-Max™ is the first product of recombinant DNA technology in the U.S. food supply.
- First insect-protected corn: Bt corn.
- First food product of biotechnology approved in U.K.: modified yeast.

1993

- The creation of the Biotechnology Industry Organization (BIO).

1995

- The gene therapy becomes a tool against cancer.

1997

- First animal cloned from an adult cell: a sheep named Dolly in Scotland.
- First weed- and insect-resistant biotech crops commercialised.
- Biotech crops grown commercially on nearly 5 million acres worldwide: Argentina, Australia, Canada, China, Mexico and the United States.

Also in the 1990's

- A biotechnology-based bio pesticide approved for sale in the United States.

2000

- The biotech crops grown on 108.9 million acres in 13 countries.
- The first biotech crop field-tested in Kenya: virus-resistant sweet potato.

2001

- The first complete map of the genome of rice.
- Development by Chinese researchers of a rice strain that could double the yield produced by normal rice strains.

2002

- A draft version of the complete map of the human genome is published.
- Biotech crops grown on 145 million acres in 16 countries: acreages growth increasing 12 percent since 2001. 27 percent of the global acreage was grown in nine developing countries.

2003

- GloFish, the first biotech pet, hits the North American market.
- Worldwide biotech crop acreage rises 15 percent to hit 167.2 million acres in 18 countries. Brazil and the Philippines biotechnological crops grow for the first time in 2003. Indonesia allows consumption of imported biotech food and China and Uganda accept biotech crops importation.
- The U.K. approves its first commercial biotech crop in eight years.
- An endangered species (the banteng) is cloned for the first time. 2003 also brought several other first-cloning, including mules, horses and deer.
- Dolly, the first cloned sheep is euthanized after developing progressive long disease.
- Japanese researchers develop a biotech coffee bean that is naturally decaffeinated.

2004

- A group of Korean researchers report the first human embryonic stem cell line produced with somatic cell nuclear transfer (cloning).
- The United Nations Food and Agriculture Organization (FAO) endorse biotech crops and states that biotechnology is a complementary tool to traditional farming methods.
- The National Academy of Sciences' Institute of Medicine (IOM) considers biotech crops as the traditional, concerning safety and risks.

Source:

Guide to biotechnology. Biotech Industry Organisation 2005-2006

1.3 Different types of biotechnology

Biotechnology is roughly divided into three main parts:

- green biotechnology
- red biotechnology
- white biotechnology

Green Biotechnology: agricultural processes

It is a very important field of modern biotechnology. The foundation of green biotech is crop improvement and production of novel products in plants, which is achieved by implanting foreign genes to plant species that is economically important. This contains three main areas:

- plant tissue culture
- plant genetic engineering
- plant molecular marker assisted breeding.

Plant tissue culture

It consists of producing in laboratory conditions a whole plant from part of it or even a single plant cell. Its advantage is rapid production of clean planting materials, e.g. banana, citrus fruit, etc.

Plant genetic engineering

This field of green biotech provides a pool of techniques allowing advantageous genes to be implanted from one organism to another. This creates improved crops, materials or even animals, e.g. soy beans.

Plant molecular marker assisted breeding

Such an area involves the use of molecular markers (selected short sequence of DNA) that is responsible for a desired trait. In this way better proprieties, such as disease resistance, can be attained.

Red biotechnology: health care processes

It uses the human body's own tools and weapons to fight diseases. Red biotechnology is of great importance in traditional drug discovery and also in creating new possibilities for treatment, prevention and diagnosis (by using new methods). Biotech medicines account for 20% of all market medicines. The continuous growth of knowledge, new discoveries and investments in this field, result in the fact that the opportunities for curing broaden too.

Cell and tissues

It is very difficult for damaged joint cartilage to regenerate in the body. Through cell therapy such defects can be repaired by growing patient's own cartilage cells.

Stem cells

Research in this field may result in treating serious diseases, like Parkinson's disease.

Gene therapy

Genetic predisposition is the most conditioning factor in many forms of cancer, and that is why identifying the gene responsible for such a disease and redirecting it can result in new opportunities to face the disease.

Improvements in diagnosis

Biotechnology offers new tools for better diagnosis and testing. This is more comfortable and less intrusive for patients, but also it is better for doctors, providing extensive information.

Genetic testing

By using genetic tests over a thousand human hereditary diseases can be identified by detecting mutations in a single gene.

White Biotechnology: industrial and environmental processes

This field of biotechnology is connected with industry. White biotech uses moulds, yeasts, bacteria and enzymes to produce goods and services or parts of products. It offers a wide range of bio-products like detergents, vitamins, antibiotics etc. Most of the white biotech processes results in the saving of water, energy, chemicals and in the reduction of waste compared to traditional methods. However, this area is not new, since such processes have been used for thousands of years in the production of wine, cheese, bread and many others.

Eco-efficient enzymes

Using eco-efficient enzymes speeds up some processes in certain chemical processes (for example, transforming one substance into another) with consuming less water, raw materials and energy than the traditional one. It is a cleaner solution for industry, with the environmental impact minimized, a better product and lower costs.

The following graph (figure 1) illustrates that the application of biotechnology instead of traditional technology is friendlier for the environment and reduces the use and costs of water and energy.

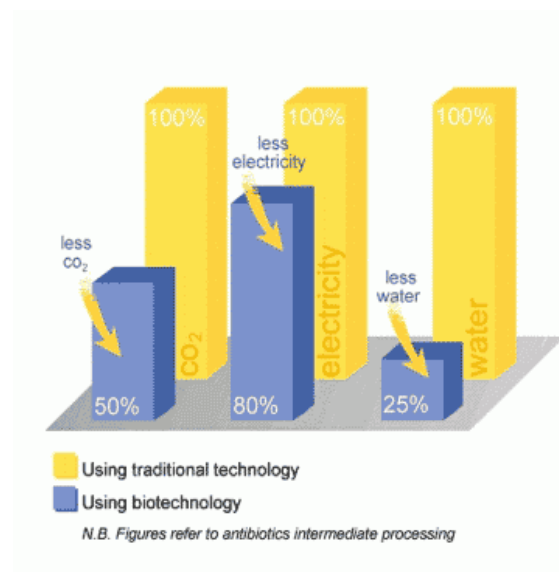


Figure 1: Biological versus traditional processing
Source: www.Europabio.org

Benign biomass

Another field of white biotech is biomass (renewable raw materials) like starch, cellulose, vegetable oils and agricultural waste that are used to produce chemicals, bio-degradable plastics, pesticides, new fibers and bio fuels, among other things. The process of manufacturing them requires the use of enzymes as well. A good example is ethanol, a renewable fuel made of biomass (it is neutral and causes no greenhouse effect).

Social acceptance of white biotechnology

White biotech enjoys a positive social acceptance because of its environmental friendly features. It provides new materials and fuels that are not obtained from petrochemical processes, improves and enhances the bioremediation of water, soils and uses less fossil-fuel energy. However, there is an issue of white biotech with a harmful impact on the biological diversity: in many of the processes defined, genetically modified organisms are used and these may be released into the environment. In order to avoid it, industrialists using them in factories, bioreactors and greenhouses are required to apply strict bio-safety regulations.

Source:
www.europabio.org

1.4 Biotech industry as a technological industry

Once the main characteristics of biotechnology as a science, together with its possibilities, have been introduced, some features of the biotechnology industry will be presented in this subchapter, basically from an entrepreneurial point of view. The importance of these factors will be developed through the project, mainly in chapter three.

As a technological industry, biotechnology responds to the following basic characteristics:

- Capital intensive
- Intellectual property-based
- Knowledge driven
- Start-ups financed by venture capitalists
- High entry barriers:
 - Patent protection
 - Solid capital basis
 - Good project management
 - Effective strategy execution to obtain fast-track regulatory approvals

Despite of being a high-tech industry, biotechnology has very particular characteristics:

- Strong influence of science
- Spontaneous division of labour in the research and productive activities
- Developments still in early stage, which offers a great number of opportunities
- Long-term product development, due to regulatory requirements
- Ethical and moral constraints

1.5 Ethical issues

Biotechnology is a very controversial subject and each type of biotech has to deal with its own ethical issues.

Stem Cells

The aim of the stem cells research is to understand the mechanism of cell differentiation and to produce specific cells from stem cell lines, and cure various diseases (cancer, diabetes, etc.). The problem is that only embryonic stem cells can be turned into any cell type. Can embryo be used as a cell producer? Is an embryo already a person?

For the moment, only embryonic stem cells – derived from frozen, fertilized eggs produced through in vitro fertilization that have not been implanted – can be used for these researches.

Cloning

Cloning is the process of genes, cells or organisms replication in a laboratory, from a single original entity. Two types of cloning can be distinguished: therapeutic cloning and reproductive cloning.

- Therapeutic cloning is used to develop new tissues that could replace damaged tissues and cure diseases such as diabetes, Parkinson's, Alzheimer's and various types of cancer and heart diseases. Indeed, the use of therapeutic cloning techniques would result in the manipulation of tissues and organs genetically identical to the patient's and, therefore, with no rejection from the body.
- Reproductive cloning is used to create copies of an existing being, leading to the hypothetical reproduction of people, born as a transplantable organ bearer.

The problem is that if therapeutic cloning is allowed, some researcher risk to make reproductive cloning that would lead to psychological and physical problem for the clone and could create a black market of usable organs.

Food and Agriculture

Agricultural biotechnology is used to modify plants and animals to import better properties to them, but their consequences are yet uncertain. For centuries, species have been crossed to produce new varieties with better properties. But is it the same as the genetic crossing of species?

There is still an additional problem of contamination: GMO's are spread easily and, if they prove to be harmful to man, as farmers claim, it will be a hard endeavour to distinguish genetically modified plants from the natural ones.

Use of Animals in Research

Before being tested on man, a lot of products are tested on animals. On the one hand, these tests permitted to develop hundreds of products that saved human lives, but on the other hand, is it acceptable animal suffering for new products' testing reasons? And who and how can decide about the necessity of tests on animals?

Ecological organizations are still fighting against big firms that rely on the extensive use of animals in their research.

1.6 Advantages of biotech

For 25 years the biotechnology sector has been experiencing an important growth because it is a very dynamic business, with a lot of challenges in new products' development to improve peoples' and animals' health quality. When a company develops a new method, they can earn lots of money over a long time period for selling their products in the market or for granting licenses and patents to other companies.

Two of the most important lines of research for biotech are DNA and genomics. Every branch of biotech – red, green and white – can profit from the results of the research in DNA and genomics, so every branch can continue its development for a long time.

For every company or research institute it is a big advantage that the research for genomics is a big issue in worldwide politics; every country wants to be a leader in this field of research. The result of this urge from governments is that they pump a lot of money into new or existing projects in companies, institutes as well into new platforms for innovations. With that the European Union is also supporting a lot of new projects.

Another reason why governments give a lot of money is the diversity of biotech in a lot of fields. For example in the Netherlands the Ministries of Economics, Agriculture, Education & Science and Health are involved in supporting the biotech sector. This is obviously a big advantage for development in the biotech sector.

The biotech is a worldwide cross-cultural sector and is not bound by one country. The advantage of this is that the development unlimited can go on. When a country forbids applying new innovations like cloning or the use of GMO's; the research will always go on in another country for example in the Asian countries for cloning and the United States for GMO's. When these countries perfected the developments it is impossible for striking countries to keep these products out of their territory because it gives so many advantages for health-improving or providing human and plants diseases that they can not ignore them.

Some advantages of biotech are:

- Reduce pollution and waste
- Decrease the use of energy, raw materials and water
- Lead to better quality food products
- Create new materials and bio-fuels from waste
- Provide an alternative to some chemical processes.

1.7 Opportunities and risks in biotech

The opportunities for biotech in the coming years depend on questions like these following:

- Are there developments in the social-cultural level where the use of biotech can be anticipated?
- How will the new technology be accepted?
- What is the national public interest?

Furthermore, biotech is one of the technology fields in which it is most complex to expect good results. Biotech is mainly characterised by two output parameters: *profits* and *people/planet*. The first parameter can be assessed through economic and financial tools but, for *people/planet* parameter there are not tangible output indicators available, so the assessment is not possible.

The main opportunity for biotech is to develop new products and services for a demanding society. Everyone in the world wants to live in a better society so there is a basis but there is also a big pressure from this society; they want to have new treatment methods, medicines, modified food, etc., as fast as possible.

Moreover, biotech opens a new door to fight against poverty: grain or maize with a better value and much better resistance against plant diseases and dryness, for example, may provide food to the third world.

Chapter 2

Characteristics and trends in biotechnology

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Chapter 2

Characteristics and trends in biotechnology

Introduction

This chapter describes the characteristics and trends in biotechnology in the four European countries for which this research is done: Poland, France, the Netherlands and Spain. At the end of the chapter, an analysis about the European Union in general, and some information about biotechnology worldwide are provided.

The structure followed to conduct the analysis of the trends and characteristics of the different countries is based on a *PEST analysis*, which focuses on the political, economic, social and technological factors that have influence on the country or organization studied.

2.1 Preliminary remark about European biotechnology legislation

Within the European Union some directives and regulations control the use and management of biotechnology products and processes, being the most important among them:

- *Directive 98/81/CE* (modifies *Directive 90/219/CEE*)
This Directive regulates the use of genetically modified organisms.
- *Directive 2001/18/CE* (derogates *Directive 90/220/CEE*)
This Directive controls deliberate release of genetically modified organisms into the environment.
- *Regulation 1831/2003* (modifies *Directive 2001/18/CE*)
This Regulation conducts traceability and labelling of genetically modified organisms, and traceability of food and feed produced from genetically modified organisms.

According to this European legislation, each country implements its own biotechnology law system. In this chapter, it is shown how Poland, France, the Netherlands and Spain adapt their biotech legislation to it.

2.2 Biotech in Poland

Political forces

There are 4 main acts obligatory in Poland:

- About ecological agriculture (March 16, 2001 published in Polish Official Journal on June 22, 2001 No.63. 634)
- About food and nourishment (May 11, 2001 published in Polish Official Journal on June 22, 2001 No.63. 634)
- About GMO (the most important) (June 22, 2001, published in Polish Official Journal on July 25, 2001 No.76. 811)
- About pastures. (August 23, 2001 published in Polish Official Journal on September 25, 2001 No.123. 1350)

In reference to the genetic modifications of the human genome and in cases relating to food and pharmaceutical products, in Poland, as in other countries of EU, specific law regulations have been implemented. The law in Poland is consistent with the European Union directives. The Government's attitude to biotechnology depends on the sector, from the acceptance of white and red biotech to the refusal of green one. There is a ban of growing GMO in the area of Poland. The conception of The Department of Environment is: Poland is an ecological country whose best value will be the production of healthy traditional food the demand for which will increase constantly.

The policy of Poland contributes to the discouragement of the society in biotech products. The position of the government is strongly replied by experts of the field.

Economic forces

World Economic Forum in 2005 in their annual ranking of competitiveness of the world's economies listed Poland in 51st position (117 classified countries).

The fundamental factors that hinder and limit external investments are: bureaucracy, tax system, difficulties in taking a credit and the attitude of the Government to innovative technologies.

Poland is not an innovative region (21st position among countries of EU according to the ranking of innovativeness). There are bad conditions for researches and development and small funds go to this field – 0.6 % of GDP – 1.14 thousand million in the year 2004.

The financing of biotechnology in Poland is a really big problem. Most firms must face the problem of innovativeness and compete with firms from abroad. Having one's own R&D department is very expensive, so cooperation with universities is sometimes the only way of outsourcing some work.

Sources of financing biotechnology in Poland:

- State subsidies
- Funds from EU
 - CRAFT
 - PHARE
- By company, but only big companies can afford expensive researches
- Venture capital

Social forces

There is a market of 39 million people. Poland has an excellent geographical location, as it is an economic bridge between the West and the East. Its strategic location between Germany and Russia gives this country an opportunity of economic and marketing perspectives.

The social acceptance of biotechnology depends on the issues. Medical applications have high social support, above 80%. On the other hand, cloning has not gained acceptance at all. People of Poland are generally against genetically modified products and they do not want to listen to the opinions and arguments of scientists and experts. The European Biotechnology Organisation made a study among Polish people. To the question “Do you eat genes?” 25% answered affirmatively, 29% responded negatively and 46% did not know. For question “Do we have genes in tomato?” 41% answered affirmatively, 19% responded negatively and 40% did not know.

Unfortunately, the society does not realize that we are the consumers not the producers of the biotech products. To illustrate the problem, it is worth presenting the following: in 2004, Poland imported about 1.5 million metric tons of genetically modified fodder for animals (corn and soy bean).

90 % of the people think that it is necessary to create legislation and the state supervision of biotechnology with EU legislations standards. Also the biotechnology and genetic engineering have to be governed by law and under supervision of state administration.

More and more people think that the public debate is needed (47% in 1999, almost 60% in 2003) but, contrary to that, the will to buy biotech products decreased from 70% in 1994 to 30-40% in 2005.

The decrease in confidence is evident and is the result of lack of actions to popularize biotech and to educate the society.

Technological forces

Poland has a high level of education in natural and engineering sciences, well educated young people, who study at 21 Polish universities.

There are several fields working on research and development:

- Pharmaceuticals
- New vaccines (particularly eatable vaccine)
- 40 experiments with GMP (in 2003 – two experiments)
- Enzymes
- Biomaterials
- Bio-fuels
- Food additives
- Protection of environment using micro organisms
- No commercial cultivation of GMP and no production of GMO

However there are some weaknesses:

- Poor transfers of new technologies from universities to industry and direct industry academia co-operation
- Deficiency of science parks and incubators
- Limited number of centres of technology transfers

Poland needs some factors that promote innovations:

- Effective structures facilitating technology transfer
 - New added value products and services – more competitive enterprises
- Suitable environment for business
 - Incubators of business development
 - Parks of science and technology
 - Parks of industry and technology
 - High risk financial support
 - Banks supporting investments
 - Legislative acts
 - Social acceptance

Sources:

- www.Biotechnolog.pl March 2006
- *Polish biotechnology* by Stanislaw Bielecki and Tomasz Twardowski

2.3 Biotech in France

With more than 200 biotechnology companies employing around 3000 people, the French biotech, mainly dedicated to the human well-being, has a quite strong position in Europe.

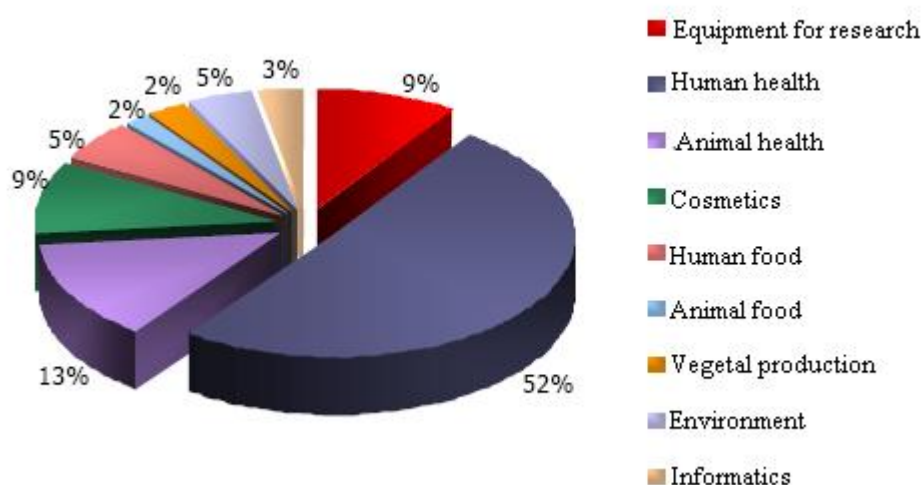


Figure 2: Distribution of French biotechnology
Source: *Rapport sur la place des biotechnologies en France et en Europe*

In 2004 the four main French companies accounted for a turnover of 115 million euros and employ 892 people.

Company	Turnover	Size
Cerep	51,3M€	450
Flamel technologies	40,6M€	222
Genfit	12,2M€	105
Biogemma	10,8M€	115

Table 1: Main French biotech companies in 2004
Source: *Rapport sur la place des biotechnologies en France et en Europe*

Political Forces

Biotechnology is the priority for the French government which spends more than 5% of the national public R&D budget on it (and mainly in the pharmaceutical and agro-food sector). To encourage biotech companies, the French government has taken several measures, among them the JEI (Young innovative company) status, consisting of tax reduction for companies that are fewer than 8 years old, spending more than 15% for their R&D department, employing fewer than 250 people and with a turnover lower than 40 million euros. It concerns about 150 companies.

Concerning the implementation of European directives, a law, related to bioethics, was voted in 2004 (LOI n° 2004-800²) which bans, for the moment, both reproductive and therapeutics cloning.

²<http://www.legifrance.gouv.fr/>

For GMOs, according to the European directive 90/220 and 2001/18 , the uses of GMO's for researches and for the industry in greenhouses are both authorized but submit to stringent rules (4 types of confinement depending of the danger of the GMO). Concerning the use of GMO's in fields, the precaution principle is applied and the authorization may be given only after a visit by government experts.

Concerning the future French biotech policy, a report³ has been prepared with 63 recommendations in 15 topics to create a law supporting biotechnologies.

Economic forces

French biotech companies have a financial problem. In fact, the number of IPO (Initial Public Offerings), which is one of the main sources of finance for a company, is worrying. A comparison between the financing of biotech companies for some countries is provided in figure 3.

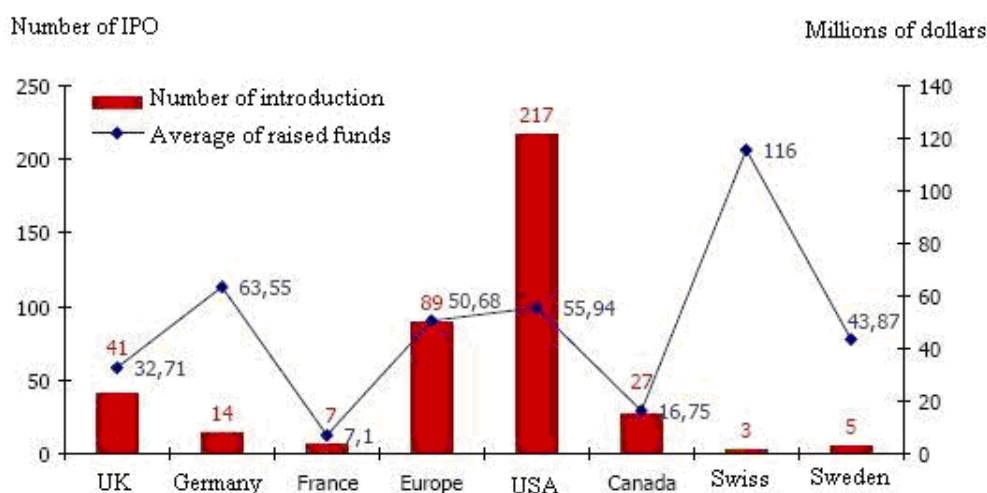


Figure 3: Number of IPO and average of funds raised between 1996 and 2004
Source: Biocentury

Whereas 2004 was promising after the 2003 crisis, the fund raised in 2005 represent only 171 million euros invested in biotech companies, which is catastrophic for the sector (figure 4).

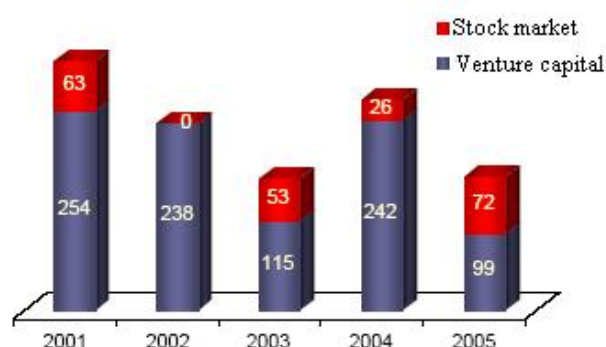


Figure 4: Fund raised by French biotech companies (million euros)
Source: *Rapport sur la place des biotechnologies en France et en Europe*

³ <http://www.assemblee-nationale.fr>

In order to face financial problems the French government subsidizes companies. Such subsidies are:

Genhomme (governmental organisation):	4.5 M€
Concours SDV (Life science contest):	7.2 M€
Incubateurs (incubators):	2.2 M€
CIR (Tax reduction for research):	28 M€
JEI (Youth innovative companies):	10 M€
Anvar (French agency of innovation):	17.6 M€

These subsidies support the biotech research but they are much lower than subsidies granted by Germany or the United Kingdom.

Trend: The future of French biotech finance could be in FCPI (a kind of share with tax reductions) or in JEIC (young innovative companies introduced in the stock market) in the creation of a support fund for biotech companies and an effort made by the government to facilitate introduction of the biotech companies in the stock market.

Social factors

The biotech sector represents about 3067 employees – including 1890 working in R&D departments – and it is quite dynamic (see figure 5).

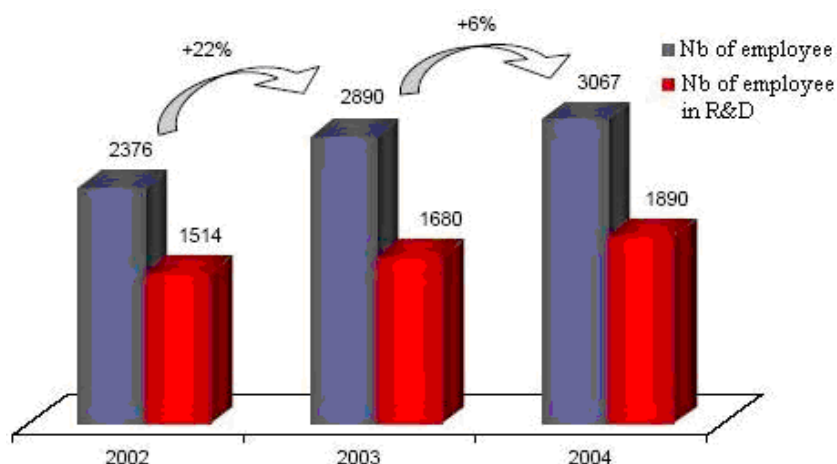


Figure 5: Employment in French biotechnologies
Source: *Rapport sur la place des biotechnologies en France et en Europe'*

Concerning GMOs, there is a suspicion from the population which is in favour of the precaution principle. Especially unions and farmers against GMOs: conducted by José Bové, the farmers confederation broke the law, destructed some GMOs yields and feeded the debate concerning GMOs in France. José Bové was sentenced to 14 months imprisonment for his acts.

Due to a pressure from the consumers, every product containing GMOs must have been indicated it on its label since 2003.

Technological forces

France has quite a strong position in the worldwide biotechnology but there is a problem of patents: 45% of the companies do not have any patents and fewer than 2% of the companies owns 80% of the patents.

Partners of French Biotech Companies are mainly French companies (58%), the rest of Europe (20%) and the USA (11%).

Conclusion

The French structure that deals with Biotechnologies is '*France Biotech*', an association that comprises 150 of the main French biotech companies.

Whereas the USA biotechnology industry is recovering from the global economic recession of the year 2000, with a strong impact on biotech, Europe has still problems (only 13% of the biotech industry investments were made in Europe in 2004). In France, financial problems are very important and it is a vicious circle: if there are no investors, the sector is going bad and investors do not want to come. To face to this problem, the French government supports biotech companies with laws and subsidies.

French biotechnology is resisting to the financing problems. However, the Government must accentuate its efforts to help the French biotech companies to innovate and survive.

Source:

- *Benchmarking of public biotechnology policy* Final report European Commission Enterprise Directorate General
- *Panorama des biotechnologies en France* by France-Biotech
- *Rapport sur la place des biotechnologies en France et en Europe* from the Office parlementaire d'évaluation des choix scientifiques et technologiques

2.4 Biotech in the Netherlands

Political forces:

Policy profile of the Netherlands

The policy profile of the Netherlands: all policy areas are involved in the promotion of biotechnology. Most policy goals and most policy areas receive attention. More than 5 % of the national R&D budget is spent on biotechnology. A broad range of sectors is addressed in biotechnology policies in the Netherlands: pharmaceuticals, agro food, chemicals, laboratory equipment and supplies and specific fields like tissue engineering.

In the Netherlands, the impact of biotech policy is assessed in the process of elaborating a new policy initiative and after the policy initiative has been implemented.

Several stakeholders are involved in the assessments: policy-makers directly involved in the elaboration of the policy initiative, representatives from industry and their business organisations, from social groups and non-expert citizens. Economic and social (such as job creation, education careers) impacts for the short term (0–5 years) are addressed in the assessments. Also the geographical dimensions are relevant as attracting foreign companies to the Netherlands is one of the issues.

Formal mechanisms for the coordination of biotechnology policy do not exist while informal do (interdepartmental group biotechnology). All European Commission directives from the project '*Life sciences and biotechnology – a strategy for Europe*' have been implemented; some of them fast and without any controversy (contained use, protection of workers), some are rather controversial like the ones on patents, GM organism, GM foods and labeling.

Dynamic changes in the policy profile

There are some interesting differences between the policy profiles in the mid 90s and now. First of all, in this time the number and size of dedicated biotechnology research programs is considerably higher, compared to the previous period. Secondly, a broad set of biotech transmission instruments was running in the period 2000–2005 that supported the creation of firms. It included a start-ups venture fund, infrastructure facilities, consulting and advisory services in management issues and IPR issues. A third important development that characterises the current profile and differs considerably from the mid 90s profile concerns the policies to exploit the regional potentials. In 2005 regional innovation policy-making gained importance. The (network of) biotechnology incubators play an important role in this respect. In six Dutch universities town's biotechnology incubators⁴ have been set up. They function as catalysts in economic development processes in the regions. Regulation was and is a high priority issue in biotechnology policy (nowadays deregulation is a topic). The same accounts for fiscal policies. They kept their high scores.

Source:

Benchmarking of public biotechnology policy Final report European Commission Enterprise Directorate General

⁴ A room that can be maintained at a constant preset temperature, used for culturing or growing bacteria.

Economic forces:

The Netherlands were in the last four years in an economic depression; it was one of the countries that had the lowest economic growth in the whole European Union. But since the middle of 2005 the economy has been growing. Conspicuous about this recession is the fact that the biotech sector collects a lot of money for new research projects or setting up new companies. That results from the will of the banks to invest in this sector. The stock exchange market was very bad in 2003/2004 so the banks were setting up funds to invest in biotechnology. This was a success for the banks (high returns to 30%) as well for the biotech companies because they have done a lot of (expensive) research and in a few years time may make profit. For example, the company *Crucell* was also a newcomer five years ago sponsored by banks and is now standing out on the Amsterdam Stock Exchange, as its exchange rate value increased from €5.30 to €21.34 (19-04-2006). Although *Crucell* took over a biotech company in Switzerland, it never has made profit due to the high costs of researching.

To hold these companies *Dutch* the banks must invest money in new researches and technologies because when a research project is finished and the patents are distributed, the company is a prey for the big companies in biotech.

Biotechnology is not a big sector in the Netherlands; only 1.6% of all the produced goods and services are from biotech⁵. This is relatively the same level as in a country like Slovenia. Belgium, the neighbour of the Netherlands, spends more to biotech as shown by the percentage, which is 3.7 %.

Technological forces:

For the last years there has been a conspicuous growth of biotech medicines introduced every year. This means that biotechnology companies interfere in the pharmacy sector. The combination of pharmacy and biotech can deliver huge possibilities to develop new technologies. Also the biotech and pharmacy sector focus on individual and personal solutions instead of the general 'blockbuster' medicines. The market is asking for these products and can also offer great opportunities for the sector.

Competitor forces:

According to the report '*Beyond Borders 2005; an overview of the worldwide biotechnology*' from accountant Ernst & Young, the competitor strengths of Europe and especially in the Netherlands is growing. This results from:

- The investments in biotechnology companies through banks and venture capitalists
- The transformation from traditional production processes to a complete new Life Sciences company. For example; the company 'DSM' produced for many years the same textile and plastics. By means of new technologies like super strength fibres the aim clients changed from national customers to high profitable worldwide clients.
- Government institutions are having more possibilities to cooperate with particular companies.
- Through these three above-mentioned points, institutions from the United States are setting up combined development programmes with Dutch companies.

⁵ Results from *Beyond Borders biotech in 2005*, Ernst & Young

2.5 Biotech in Spain

Political and legal forces concerning biotechnology:

Legislation regulating Biotechnology::

European Directives and Regulations concerning biotechnology are incorporated into the Spanish legislation through the following Laws and Decrees⁶:

- *Ley 9/2003*
This Law regulates deliberate release and commercialization of genetically modified organisms.
- *Real Decreto 178/2004*
This Royal Decree gives application to the contents of the EU Directives not considered by the *Ley 9/2003*.
It contemplates all the necessary aspects for the effective application of the Law: requirements and procedures for the accomplishment of the activities of confined use, deliberate release and commercialization of genetically modified organisms; norms on information, vigilance and control of these activities; responsibilities; infringements and sanctions; as well as the competences of the Interministerial Council of Genetically Modified Organisms, and of the Biosafety National Commission.
- *Real Decreto 1477/2004*
This Royal Decree conducts the development of the basic organic structure of the Ministry of Environment

Spanish institutions responsible for Biotechnology:

- *Interministerial Council of Genetically Modified Organisms;*
The authorizations corresponding to the State General Administration are conferred by the Interministerial Council of Genetically Modified Organisms. It depends on the Environment Ministry and works in coordination with the National Commission of Biosafety, and is responsible for the coordination and exchange of information with Spanish regions and with the European Commission.
- *National Commission of Biosafety;*
It is a consulting organ whose function is to inform about the authorization solicitudes corresponding to genetically modified organisms.
This Commission depends on the Environment Ministry and it is composed by the representatives of the different Spanish regions, as well as by people and institutions experts on the matter.

Source:
www.mma.es

⁶ It has been considered to keep the original names of Spanish Laws and Decrees, with no translation of them into English. "Ley" means Law, and "Decreto" means Decree. When the Decree has been issued by the King it is named "Real Decreto" (Royal Decree).

Economical forces concerning biotechnology

Spanish economy's highlights:

- Population: 43.5 million inhabitants
- Spanish economy grows 3.5% annually
- GDP (Gross Domestic Product): €0.95 trillion
- GDP per head: €21,800
- Number of companies: over 2.5 million (including medium-sized businesses and freelancers)
- Number of employed people: over 17 million
- Inflation (may 2006): 2.7%

Biotechnology companies in Spain⁷:

- Companies Fully Devoted to Biotechnology (CFDB)
 - Biotechnology accounts for over 80% of their activities.
 - Biotechnology accounts for over 50% of their turnover.

In 2004, there were 102 CFDB (just one out of every 15.000 companies) in Spain, employing 1.800 people in total (a little over one out of every 10.000 jobs) and with a turnover of around 400 million euros (only five euros out of every 10.000 euros of the GDP).

- Companies Partly Devoted to Biotechnology (CPDB)
 - Although some of their main business lines are biotechnology-related, biotech accounts for less than 80% of their activities.
 - It can be inferred that, on average, biotech activities account for around 8% of turnover of CPDB. These percentages, however, vary a lot between companies in different biotech branches (from 5% in food and agriculture to 66% in IT or R+D services).

In 2004, there were 114 CPDB in Spain, employing 19.000 people and with a turnover of around 6.800 million euros (which is close to 1% of the GDP).

- Companies that Use Biotechnology (CUB)
 - Some of their main business lines are biotechnology-based.
 - Part of their turnover is biotechnology-related.

In 2004, there were 100 CUB in Spain.

- Biotechnology Industry Service Companies (BISC)
 - Auxiliary services: consultancies, advisers, bioinformatics, etc.
- In Spain, in 2004, there were 51 BISC.

Source:

Spanish Biotechnology: economic impact, trend and perspectives.

- Chapter 2: The situation of Biotechnology in Spain.
 - Chapter 4: Macroeconomic relevance and forecasts for the future of Biotechnology in Spain.
- Spanish foundation for the development of genomic and proteomic research, Genoma España; June 2005*

⁷ *Genoma España* from data provided by the Commercial Register, the Nacional Statistics Institute and own databases.

Social trends concerning biotechnology

The Spanish society's attitude towards biotechnology is more optimistic and favourable than the European average. The applications with the greatest social impact relate to cloning, transgenic food, the medical implications of biotechnology, the discovery of new genes and genome sequencing.

Let's look at the results a survey conducted by the electronic edition of one of the most widely read newspapers in Spain. To the question "Do you agree with therapeutic cloning?" about 65% responded affirmatively, 33% negatively and about 2% did not respond.

The reply to the second question raised by the newspaper was just the contrary: "Do you agree with reproductive cloning?" – 39% yes, 59% no, 2% did not know –.

Sources :

Spanish Biotechnology: economic impact, trend and perspectives.

- Chapter 2: The situation of Biotechnology in Spain.

Spanish foundation for the development of genomic and proteomic research, Genoma España; June 2005

www.lavanguardia.es; digital newspaper from Spain

Technology situation concerning biotechnology

According to scientific production indicators, biotech research in Spain is mainly basic; there is more focus on the provision of services than on the development of products.

The fact that Spanish research does not focus either on applications or developments, is illustrated by the important gap between the generation of knowledge and the production of patentable applications in Spanish biotechnology.

By 2000-2003, the Spanish contribution to world scientific production relating biotechnology was in the fourth position within the EU-15, only after the United Kingdom, Germany and France, and closely followed by the Netherlands and Italy, which proves the international competitiveness of the scientific component of Spanish biotech. By contrast, Spanish biotech researchers contribute approximately only with 0.47% to European patents applications.

Furthermore, "the scientific publications of 40% of Spanish biotech research groups are a basic reference for American patents applied for by US companies and researchers, in particular for biotechnology applications in the fields of human health, industry and food and agriculture"⁸.

Source:

Spanish Biotechnology: economic impact, trend and perspectives.

- Chapter 2: The situation of Biotechnology in Spain.

Spanish foundation for the development of genomic and proteomic research, Genoma España; June 2005

⁸ Excerpt from *Spanish foundation for the development of genomic and proteomic research*; Genoma España; June 2005.

Forecasts for the future⁹

- Spanish biotechnology will not catch up with EU-15 biotechnology for at least 20 years, and it will take over 30 years to catch up with the US. Convergence is unlikely to happen under the current investments and state-of-the-art conditions.
- The most significant social and economic impact of biotechnology for the next 15 years will be on health and quality of life, followed by technological innovation and industrial research.
- There will be many genomic applications in the areas of health, environment and agriculture by 2010. Pharmaceutical innovations will be based on genomics and genetics.
- The biotechnology market will grow in value by 14% annually between 2004 and 2015. The markets that will contribute the most value will be, in order of importance, agriculture, materials, human health and the environment.

⁹ Excerpt from *Spanish foundation for development of genomic and proteomic research*; Genoma España; June 2005.

2.6 Biotech in Europe

How important is Europe for biotechnology?

It is very important because almost all the rules come from Brussels but Europe as well, also because of the main subsidies come from Europe. With this money will research power of all EU members be bundled and a substantial part of the biotechnology research will be financed.

The other way round, biotechnology is very important for Europe. It is a technical high-quality activity that makes opportunities for better healthcare, farming, food production and improvement for the environment. In this connection biotech plays an important role in the Lisbon Strategy, as exposed in the annex.

Financial results European biotech

After some years with reconstructions and scarce development the biotech sector in Europe in 2005 has good results¹⁰. Comparing to the United States the number of new biotech companies on Stock Exchanges in Europe was bigger; 13 companies in the US against 23 companies in Europe. The result of this improving Stock Exchange climate is that the European biotech gets more new capital than the United States; €3.2 million against €2.1 million in the US. When the turnovers of biotech will be compared of the two continents, Europe remains a poor player in the worldwide biotech market; only 15% of all biotech turnovers against 75% in the US.

A conspicuous point is that the biotech sector worldwide decreased their loss in research and development to \$4.4 billion in 2005 against \$8.9 billion in 2004 but the biotech sector worldwide is still not profitable. They expect that in 2008 the sector can write black marks on their result bill. The reason for these big losses is that the research and development route can take a lot of years before an idea can be introduced into the market and make profit. For example the average time for R&D in medicines is seven years. And with a lot of research projects it is insecure if the new ideas will be finished with the result that the whole route was financial unprofitable.

¹⁰ Results from 'Beyond Borders' biotech in 2005, Ernst & Young

2.7 Information about biotech worldwide

- The United States, the world biotech leader, with 78% of global turnovers in this industry, will keep its position as 80% of all risk capital in the US is moving to biotechnology companies.
- Europe has as many biotech companies as the US (1.700) but the companies in the US are much bigger; this makes the companies in Europe much more vulnerable when the economy is in a depression. Examples of big American companies are: Genentech, Biogen, Genzyme, Amgen and Monsanto. Europe has only one company of that size, namely Sorono from Switzerland¹¹.
- Asia will become a big player in biotechnology because of the repulse of poverty, availability of food and creating employment, high-qualified employment will come from Europe, and due to less restrictive law.

¹¹ Elsevier magazine February 2006

Chapter 3

Innovations in biotechnology

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Chapter 3

Innovations in biotechnology

Introduction

At this point of the project the concept of biotechnology has been introduced, as well as its situation in Europe. In the first chapter the main characteristics needed to fully understand biotechnology have been provided: its definition, main historical facts, and different fields embraced by biotechnology together with their most relevant applications, and finally, some aspects that have a strong impact on it, such as ethics and moral. Concluding the chapter, some advantages, risks and opportunities are exposed.

The main purpose of the second chapter is to depict the macro-environmental factors conditioning biotechnology. Bearing this idea in mind, the political and legal situation, the economic and social factors, and technology availability and trends have been developed for Poland, France, The Netherlands and Spain, to expose how extended is biotechnology in such countries, and how do they tackle with it. At the end of the chapter some conclusions for the situation of biotechnology in Europe and worldwide are provided.

Once the concept of biotechnology and its background have been presented, the aim of this chapter is to present how the innovations in such industry are managed, which is, by the way, the core of the project. Therefore, the chapter begins with a theoretical exposition of innovation, its definition and main characteristics. This introduction is followed by a brief analysis of the situation of innovation in the countries on which the project mainly focus; Poland, France, The Netherlands and Spain. After the presentation of the main characteristics and situation of innovation, the concept of the value chain is developed: starting from a general and theoretical point of view and then leading the exposition to the biotechnology value chain. Afterwards, the chapter focuses on the biotech industry and some concepts and activities deriving from it. At the end, patents' main characteristics and their importance in an industry such as biotechnology are presented.

3.1 Innovation

Nowadays, companies must innovate in order to survive. Subjected to a very high pressure, because products and processes' life cycles are becoming shorter and shorter, companies that do not innovate are caught up by their competitors. This situation is particularly important in the biotechnology industry. On the one hand, biotech, as a high-tech industry, experiences acute shortages of life cycles due to the continuous improvements of current technologies. On the other hand, as a knowledge-driven industry with a strong dependence on science, companies' success is closely to with the efforts made in creating knowledge.

- **Technical progress**
The effort invested in improving and developing new technologies brings about the appearance of new products with better properties. As stated above, it is basic for biotechnology companies, since new biotech products development virtually always requires new knowledge and technologies.
- **Internationalization of the economy**
Competitors can appear from all over the world, not only from local or neighbour countries. How important this factor is for biotechnology can be easily understood through the conclusions delivered by the first chapter regarding the biotech market worldwide: Asian technology market, for example, is growing at an astonishing speed.
- **Markets based on individual desires**
There is a trend to produce more personalized products, focused on specific markets.

It also important to remark that, with the formulation of the Lisbon Agenda by the European Commission in 2000, innovation becomes a crucial way for achieving high economic development and growth.¹² Furthermore, architects of the Lisbon Agenda believe that the 21st century economy will be based on knowledge and on its management, therefore the role of biotechnology and life sciences in this economy is particularly relevant. An outline of the ideas delivered by the Lisbon Agenda is provided in the annex.

1. The life cycle

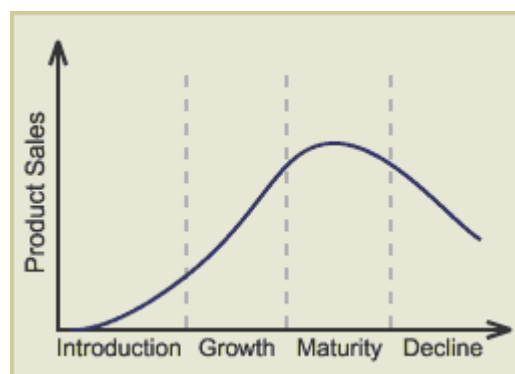


Figure 1: Product life cycle

¹² *Innovation Definition. Comparative assessment.* Draft from the European Commission Communication; Brussels, 2005.

A new product or process, progresses through a sequence of stages from its introduction into the market to its death, known as its *life cycle*, associated with changes in the marketing situation.

- Introduction stage: In the first stage sales grow slowly. The product is just being introduced and customers are unconvinced. Probably some technological deficiencies are not solved yet.
- Growth stage: In the second stage the product is increasing its market acceptance. Sales growth is accentuated. New manufacturers decide to produce the same product.
- Maturity stage: In this stage the market is fairly saturated. The battle between competitors is focused on prices and differentiation.
- Decline stage: Decrease in the number of customers and sales. New products on the market are offering better qualities.

Biotechnological and pharmaceutical products' life cycles are quite particular. The resources to invest in the development of a new product before its introduction stage are extremely high, especially on economic resources, time and knowledge. Besides, the technology required to develop such research is also severely demanding. Once the product is launched into the market, its life cycle has also some particularities. Biotech products are patented. So in many cases, it is difficult for them to find products with which having to compete directly. So, in a way, their life cycles are strongly influenced by the life of the patent. The example of some pharmaceutical products in Asian market shows this situation¹³: *the generic pharmaceutical market in Asia is at its growth stage. One of the main factors is the patent expirations of some 47 blockbuster drugs in the next five years, what provides opportunities for manufacturers to produce generic versions of the drugs.* As illustrated by the example, the more years the product remains patented in the market, the longer their maturity stage will be. When the patent of the product expires, it enters into its decline stage, as lots of products with the same properties get into the market for a much lower cost.

2. Continuous changes in technology

When the research on a technology is just started the progress is very slow. However, once the main problems are solved, with a small additional expenditure, profits experience an important boost. After this stage the growth steadies: the company needs to spend more than in the previous stage to keep the same progress rate, or a lower progress rate has to be accepted. At this stage of stagnation the technology is near its limit, so a radical change should be considered. In the early phases after such change progresses may happen very slowly but, in the future the new technology may be better than the one abandoned. This behaviour is illustrated by the Foster's S curve (Figure 2).

¹³ *The generic invasion – An inside Scoop to the Pot of Gold*, March 2003; www.biotech.about.com

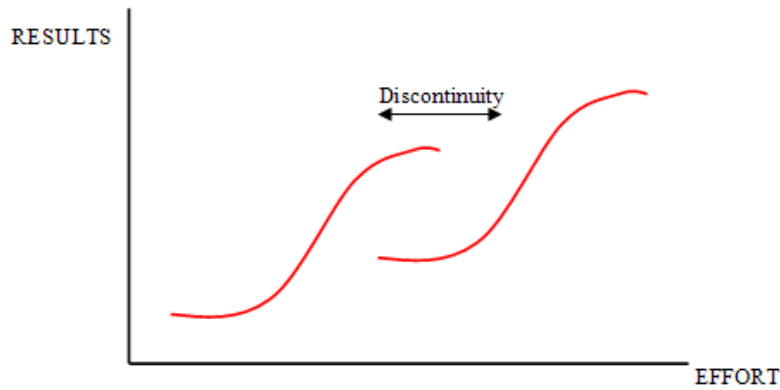


Figure 2: Richard Foster S curve
Source: *Innovation*; Richard Foster 1986

The progression of a technology through its S curve is parallel to its life cycle. As shown in the figure 3, the S curve represents three stages of the technology's state: embryonic, growing and mature. When the technology is mature, that is to say, before its life cycle reaches the decline stage, a substitute technology need to be developed.

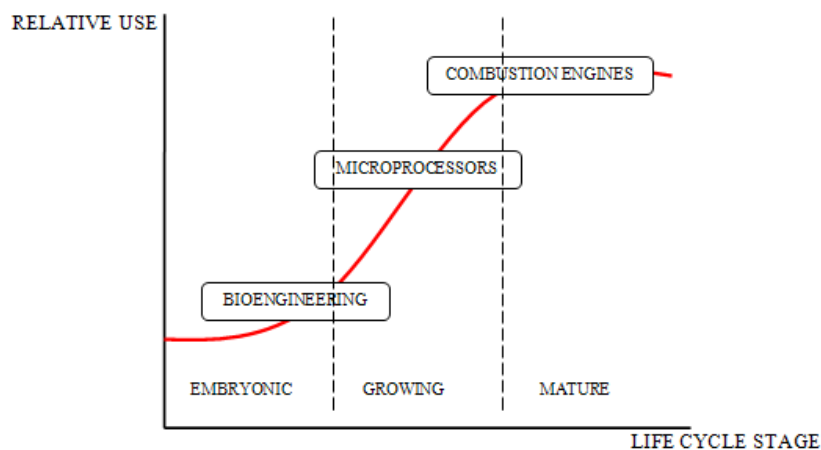


Figure 3: The life cycle of technologies

Figure 3 illustrates the maturity stage for three different technologies. Bioengineering, used in some fields of biotechnology, is still in its embryonic stage: it offers many opportunities to companies to develop new products or processes. However, due to its very high entry barriers – patent protection, solid capital basis, knowledge driven, good project management –, not a single company can get into such market. As illustrated in figure 3, microprocessors' technology is at a growing stage: everybody in the western world use devices containing microprocessors. Combustion engines illustrate the condition of a technology at its mature stage. With regard to engines, and as an example of the relevance of the changes in technologies, lots of new developments are undertaken in the sector: hydrogen engines may be seen as a technology aiming to substitute traditional combustion engines (a new S curve).

3. Innovation definition

At the beginning of the project, in the first chapter, it was exposed how difficult it is to provide an exhaustive and concise definition of biotechnology, as it is an extremely wide field, including many different applications and markets. When having to deliver a suitable definition of innovation a similar problem arises. The concept of innovation is seen from an eminently theoretical perspective in the academic background, and from a practical point of view in industry. Furthermore, even within industry, the idea of innovation is not the same for traditional industries as for high-technology companies, for example. Some definitions are provided next aiming to offer a comprehensive view of innovation.

Five different types of innovation can be distinguished¹⁴:

- New products
- New methods of production (or processes)
- New sources of supply
- The exploration of new market
- New ways to organize business

Most of the definitions focus on the two first types of innovation: *new products* and *new processes*, as their effect on the economy is more direct. This can be applied to biotechnology. However, from a general perspective beyond biotechnology, innovation should not be reduced only to these two types, as innovation can happen without any change in either products or services: self-service shops, leasing (financial innovation) and franchise system are examples supporting this fact.

3.1.1 Innovation definitions

- Technological product and process (TPP) definition

Technological product and process (TPP) innovations comprise implemented technologically new products and significant technological improvements in products and processes. A TPP innovation has been implemented if it has been introduced on the market (product innovation) or used within a production process (process innovation). TPP innovations involve a series of scientific, technological, organizational, financial and commercial activities. The TPP innovating firm is one that has implemented technologically new or significantly technologically improved products during the period under review.

This definition was proposed by the OECD, European Commission and Eurostat in the guidelines for collecting and interpreting technological innovation data (Oslo Manual). It is a base framework for innovation definitions in the EU states.

¹⁴ Schumpeter, J. (1934); The theory of Economic Development; Harvard University Press; Cambridge; Massachusetts.

- Technological and commercial innovation definitions

According to the National Institute of Standards and Technology, an agency of the US Commerce Department's Technology Administration, two types of innovation can be distinguished: technological and commercial.

***Technological innovation** is the successful implementation (in commerce or management) of a technical idea new to the institution creating it. A **commercial innovation** is the result of the application of technical, market or business-model ingenuity to create a new or improved product, process or service that is successfully introduced to the market.*

- Broad US innovation definition

Innovation is a process through which the nation creates and transforms new knowledge into useful products, services and processes for national and global markets – leading to both value creation for stakeholders and higher standards of living.

This US innovation definition, created by the 21st Century Innovation Working Group in the National Innovation Initiative paper (2004), can be compared in the most appropriate way with the OECD and European Union definition.

3.1.2 Innovation and inventions

It is important to highlight the difference between *innovation* and *invention*: an invention is the first occurrence of an idea for a new product or process, while the innovation is the commercialization of the invention.

INNOVATION = INVENTION + EXPLOITATION¹⁵

If new products, processes or services gain no acceptance of the market, innovation just does not exist.

The biotechnology industry is mainly based on research, and therefore, inventions are continually released, and most of them registered or patented (the patentability of the inventions, and the patents themselves, are exposed at the end of the chapter). Not all of the patented inventions are transformed in a product able to reach the market, as the requirements that biotech products have to accomplish are extremely strict. Such inventions cannot be considered innovations.

¹⁵ *Tecnología e innovación en la empresa*. Pere Escorsa, Jaume Valls. Edicions UPC. 2003

3.2 The innovative process

Innovation is a very complex activity, with a huge number of components interacting. To study the process experienced since an idea is born until it reaches the market, some authors have created models to illustrate the phases to follow in this process.

3.2.1 The linear model

According to the linear model, the innovative process starts with basic research, followed by applied research and technological development, and ends with the marketing and the launch to the market.

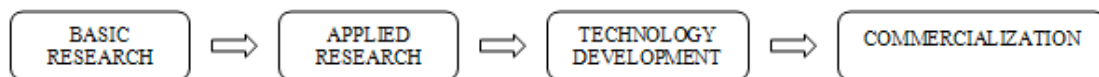


Figure 4: The linear model of innovation

Innovation and R&D:

- *Basic research* comprises all those original tasks aiming to acquire new scientific knowledge. Its results are published in scientific magazines and do not intend to reach any lucrative objective.
- *Applied research* consists of original work developed to acquire new scientific knowledge focused on practical determined goals. Applied research results in certain products (*inventions*) susceptible to be patented.
- *Technological development* embraces the use of scientific knowledge to produce materials, procedures, systems or new services, or substantial improvements. Its main goal is to launch to the market new items or determined improvements.
Through technological development, the company that acquires a patent continues with the process until the product can be launched into the market.

The linear model is fairly representative of the innovation process undertaken in the biotechnology industry: because of its strong influence of science, biotech industry largely depends on R&D. However, generalizing such a reduction of innovation to R&D is inaccurate, as for other traditional industries lots of innovations do not start from research; therefore generalizing the linear model is not realistic. Moreover, small and medium size companies cannot afford basic or applied research, due to their excessive costs. After all, even for such companies it is possible to have the best technology available without doing research, through technology acquisition, with the advantage of fast availability without all those substantial risks inherent to own research. However, such companies will never be pioneers in the market.

To represent more accurately and comprehensively the innovative process, the use of non-linear models is necessary.

3.2.2 Non-linear models

- Kline's chain-linked model¹⁶

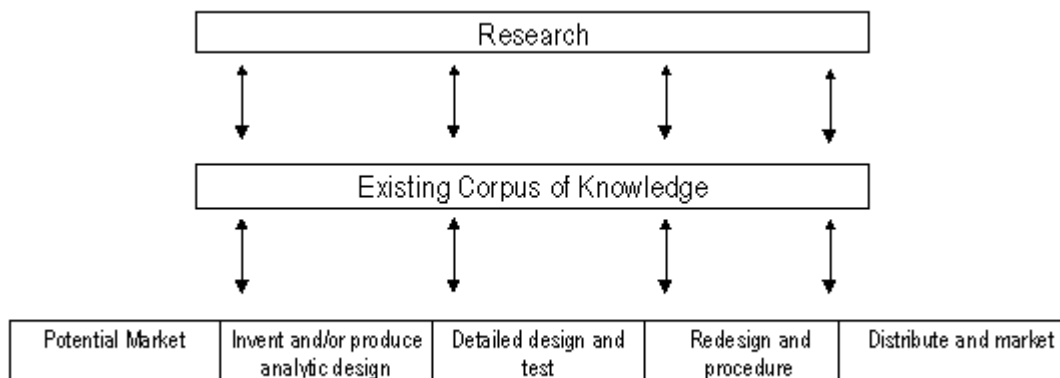


Figure 5: Kline's chain-linked model (1985)

This particular model, and in general non-linear models, shows that there are multiple paths from which innovations may arise, apart from R&D: research is not normally considered to be the initial step, as it occurs in and contributes to all phases in the innovation process. Non-linear models contain many forms of feedback.

The Kline's model combines different types of interactions:

- 1) Concerning processes within the company.
 - a. At the level of the firm, the innovation chain is visualized as a path starting with the perception of a new market opportunity (market pull) and/or a new science and technology-based invention (technology push). This is necessarily followed by the analytic design for a new product or process, and subsequently leads to development, production and marketing. Thinking of biotechnology industry, new ideas are mainly led by the development of new technologies. (The concepts of 'market pull' and 'technology push' are developed in the next point in the chapter).
 - b. Feedback relations are generated: short feedback loops link each downstream phase in the central chain with the phase immediately preceding it and long feedback loops link perceived market demand and product users with phases upstream. Problems identified by the processes of designing and testing new products and new processes often lead to research in engineering disciplines but also in science.
- 2) Expressing the relationship between the individual firm and the scientific and technical knowledge base and with research. The uses of science and technology by companies can be classified mainly in two groups:
 - The use of available knowledge.
 - The work undertaken to correct and add to that knowledge.

¹⁶ Darius Mahdjoubi; Stephen's Kline's chain-linked model. Non-linear models of technological innovation. http://www.gslis.utexas.edu/~darius/non_md1/non_md1.html

The generation of new ideas or inventions in biotechnology has a strong dependence on the knowledge (state of scientific knowledge) and on the technology available. Therefore, the better the knowledge and the technology available, the more products can be created to satisfy market needs. At the same time, the aim to satisfy the needs of the market generating new and best products brings about the generation of knowledge and the improvement of technologies.

Only large biotech firms can integrate the whole innovative process, as the resources needed are extremely huge. In order to be competitive, small and medium size companies focus on different stages of the innovative process. This idea is developed further in the chapter, where the concepts of the value chain and the outsourcing of value chain activities are defined.

In contrast to the linear model, on the same pathway as Kline's model, CIDEM's innovation model (Figure 6) states that R&D is not sufficient to accurately define the innovative process, as it is necessary to act simultaneously in other fronts, such as: generation of new concepts, product development with the shortest time to market, constant redefinition of production activities and also sales processes, with a constant feedback between them and conditioned by the knowledge and technology capability. All decisions taken derive from market needs.

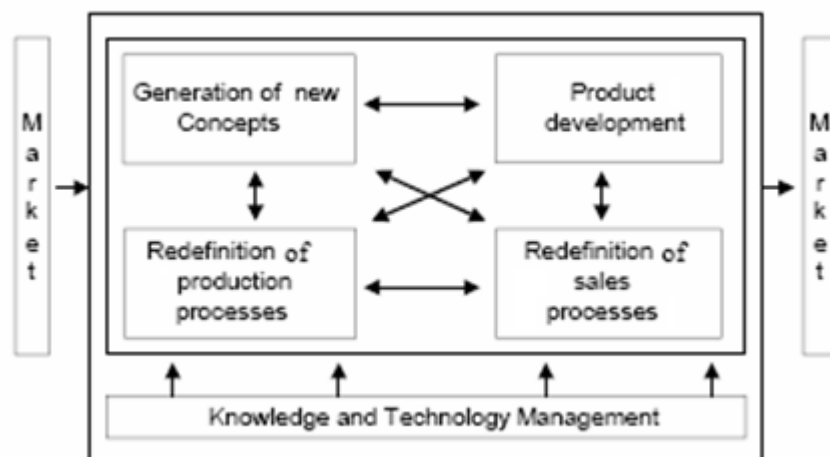


Figure 6: CIDEM's innovation model¹⁷

Despite the obvious benefits offered by doing research, it is a complex decision to determine the level of a company's resources to invest in R&D: over the last decades the costs of R&D have exponentially grown and the pace of technological change has quickened. Moreover, the assignation of resources to R&D causes the reduction of the company's immediate income. To illustrate this situation the following fact is exposed: in 1970, the development of a new medicament took on average 6 years. Fifteen years later, it had increased to 12, due to growing safety requirements. The same happens, for example, in fields such as aerospace and biotechnology. Because of the enlargement of the time required to develop the product, the profitable life of a patent in the pharmaceutical industry has suffered a reduction from 20 theoretical years to only 8 effective years (patents are presented at the end of the chapter)

¹⁷ CIDEM: the Centre for Innovation and Business Development Model of the Ministry of Industry, Trade and Tourism of Catalonia

3.3 Commercialization strategies

When creating innovations in high technology companies it is necessary to define an effective commercialization strategy, that is to say, the process by which the innovation is brought into the marketplace. The crucial element of a firm's commercialization strategy is whether it competes or cooperates with established firms.

But what makes the difference between the commercialization strategies in every field in high technology? These are the differences in the *commercialization environment*; the microeconomic and strategic conditions a firm faces when turning an "idea" into a product. This determines the most effective commercialization strategies and is the source of the different competitive dynamics in high-technology sectors.

There are two key elements of the commercialization environment;

- The intellectual property regime and
- Established firm ownership over complementary assets.

Examples of *established firm ownership over complementary assets* are manufacturing expertise or distribution channels and these two elements drive the choices and strategies of effective start-up innovators. Specifically, the widespread availability of formal intellectual property, combined with substantial expertise in regulation and distribution on the part of established players, makes transactions in the "market for ideas" an effective commercialization strategy for most biotechnology innovation¹⁸.

Though some analysts lament that biotechnology companies' lack success in integrating forward and competing with established firms, long-term competitive advantage for most biotechnology firms may be best ensured by developing ideas alongside strategic cooperation with downstream commercialization partners.

To distinguish biotechnology innovators from the establishment they must create a new managerial agenda with two main points:

- a. Managers of both start-ups and established firms must develop and implement strategies that take advantage of the commercialization environment facing start-up innovators.
- b. Innovators must build their competencies for an environment where advantage need not to be at the expense of the advantage of established firms. In other words, managers must learn that advantage derives not from the ability to disrupt established firms, but from the ability to offer a new and compelling value proposition for health care and agricultural consumers.

¹⁸ *Managing Innovations; Commercialization strategies for Biotechnology*
Joshua S. Gans and Scott Scern, February 2002

3.3.1 Contracting

Contracting and cooperation with established firms continues to be the norm. As Carl Feldbaum, President of the Biotechnology Industry Organization (BIO), succinctly remarked “strength...is reflected in the proliferation of collaborations and partnerships, which are the lifeblood of biotechnology, as indeed many of you wellknow given the phenomenal, almost exponential growth in biotech deals in recent years. For example in the year 2000, there were five times as many new deals between biotechnology companies and pharmaceutical companies as in 1993.

3.3.2 The commercialization environment

How should ideas be managed? As already mentioned before, there are two strategic options for start-up innovators:

- a. Developing a value chain from scratch allows the innovator to enter the product market and compete directly with more established players.
- b. Strategic cooperation with more established players – whether through licensing, an alliance or partnership, or perhaps even outright acquisition.

The big advantage of the latter choice is that the innovation can be directly integrated into an already functioning value chain but it eliminates the possibility of displacing the established value chain by innovation.

For most start-up innovators, the commercialization environment includes two elements crucial to the choice of commercialization strategy:

- a. The relative cost and profitability of pioneering a new value chain compared to building upon an established value chain.
- b. The knowledge upon which the innovation is built can be controlled even after the established firm becomes aware of the new technology.

According to *Gans* and *Scern*, these factors determine the potential for advantage under a cooperative or competitive strategy, shaping optimal commercialization strategy.

3.3.3 Choosing the commercialization strategy

In order to identify an effective commercial route it is necessary to find the interaction between the two known dimensions of the commercialization environment: the level of control over complementary assets, and the knowledge embedded in the innovation.

		Do incumbent's complementary assets contribute to the value proposition from the new technology?	
		No	Yes
Can innovation by the start-up preclude effective development by the incumbent?	No	The Attacker's Advantage	Reputation-Based Ideas Trading
	Yes	Greenfield Competition	The "Ideas" Factory

Table 1: The commercialization strategy framework

The commercialization strategies proposed in table 1 are described below:

- *The attacker's advantage*

This is a field between start-ups and established market leaders. While competitive commercialization does not require duplicative investment by the start-up (the established firm does not control the key complementary assets), the new technology can be easily imitated once the market leader recognizes the threat. In this environment, technological leadership is likely fleeting, and competition is likely to be intense. The development of new technology offers continual opportunities for start-ups to attempt to undermine existing market leadership; however, easiness to imitate means that most start-ups will only appropriate a very small share of the value created by their innovations. In this environment, effective commercialization strategy requires tight integration between research and commercialization.

- *Ideas factories*

Not only does the start-up innovator need to undertake duplicative investments to compete, but negotiations with the market leader need not undermine their basis of advantage. Effective commercialization strategy here results in the emergence of “ideas factories”. These are technological leaders focusing on research and commercializing through reinforcing partnerships with more downstream players. The key issue in this field is not whether to pursue a contracting strategy but when and how. Rather than disrupting their advantage, ideas factories reinforce the basis of advantage for established by firm offering a fertile source for new innovation. A supply relationship with these specialized technology producers enhances competitive advantage, particularly when the ideas factory develops technology complementary to the existing value proposition.

The ‘Idea factories field’ comes closest to capturing the origins of commercialization strategy and industry dynamics in the biotechnology and pharmaceutical industries over the past quarter century but on the other hand many new biotechnology firms, often formed around the fruits of basic research in the university sector, find it easier to discover new technology than to manage the commercialization process, including the severe regulatory hurdles, manufacturing requirements, distribution and branding.

- *Reputation-based ideas trading*

Start-up innovation in this environment may be encouraged by a market leader who commits to avoid the temptation of expropriation. The key to commitment is reputation. Rather than exploiting all opportunities for a gain in each transaction, a market leader offering a “fair” return to innovators can develop a reputation over time. This soft bargaining strategy by a market leader both encourages start-up innovation and makes themselves the most attractive potential partner for externally developed technology.

- *Greenfield competition*

This is a favourable position for the start-up innovator, since returns on the product market will be high (imitation is difficult), but a potential market power offers a substantial bargaining power with potential partners. Start-up innovators face tremendous opportunities in this environment, since they are unconstrained by past investments and so may consider multiple strategies for earning returns from innovation. However, it is important, even crucial, to note that such a favourable environment is the exception and not the norm.

Conclusion for start-up innovators

For most biotechnology companies that are often operating in environments characterized by complementary asset control by established firms alongside effective protection of the knowledge underlying their innovations – the origins of advantage most likely lie not in integrating forward into established markets but developing a core competence at innovation – building an efficient and effective “ideas factory.”

In most cases, then, the key issue is not so much whether to cooperate with more established firms but how to position the technology to maximize the return on innovation.

Though offering an extraordinary promise and value, the record of competitive advantage in biotechnology has been mixed. Despite some lament, the inability of biotechnology firms to integrate forward and compete with established firms, the most likely basis for advantage is strategic cooperation with commercialization partners. As innovation and commercialization become increasingly global and intellectual property rights are expanded to allow firms for more nuance in protecting their inventions, biotechnology managers must focus on their core competence – producing radical new technologies which dramatically improve biotech products. Perhaps ironically, the managerial agenda for biotechnology managers must be premised on a simple insight: advantage for most biotechnology innovators requires cooperating with precisely those firms who might have been their biggest competitor.

3.4 Types of innovation

- Disruptive or radical innovations

Disruptive innovations consist of a breakthrough with regard to the preceding state of the product or process. These innovations cause spectacular improvements in the results of the product or process, slightly affecting to the costs. In general, the origin of radical innovations lies in science and technology progress: *technology push* innovations.

- Incremental innovations

Incremental innovations consist of improvements in the existing products or processes. They aim of these innovations is to reduce costs. Incremental innovations usually derive from market needs: *market or demand pull* innovations.

As introduced before in this chapter, the biotechnology industry is mainly *technology pushed*: although the final objective is to satisfy market needs (*market pull*), there is no way to do this if the technology and knowledge available are not sufficient to develop these products sought by customers. Furthermore, it is also noticeable that in biotechnology the concepts of disruptive and incremental innovations overlap many times. Thinking of the development of new drugs, a company may be testing a molecule already used in a medicament, to improve its effects on the patient (incremental innovation), when realizing that the molecule can be used to treat more effectively other diseases (disruptive innovation). Illustrating this fact, in pharmaceutical industry 60% of research projects develop drugs that were no initially foreseen¹⁹

¹⁹ *Tecnología e innovación en la empresa*. Pere Escorsa, Jaume Valls. Edicions UPC. 2003

3.5 Innovations in the European Union

After the concept of innovation and its main characteristics have been demonstrated, a brief analysis of the situation of innovation in some European countries is developed. Once again the countries within the scope of the analysis are Poland, France, The Netherlands and Spain.

The analysis is based on the results issued by the European Innovation Scoreboard (EIS)²⁰, which is an instrument developed by the European Commission, under the Lisbon Strategy, to evaluate and compare, through a list of innovation indicators and trend analysis, the innovation performance for all 25 EU Member States, as well as for Bulgaria, Romania, Turkey, Iceland, Norway, Switzerland, the US and Japan. The latest publication was in 2005.

POLAND

- Poland's overall performance in comparison with other countries is rather bleak.
- The level of investment in innovation is rising.
- One of the major problems is that Polish companies do not sufficiently invest in innovation.
- The strategy for developing innovation is mainly focused on the development of R&D and on technological innovation in the private sector.
- By 2006, the total R&D expenditure was of 1.7% of the total Gross Domestic Product (GDP).
- 2005 EIS Summary Innovation Index (SII) Rank: 21.

Opportunities:

- The level of investment in innovation in the manufacturing sector increased from 3.18 billion euros in 2000 to 4.01 billion euros in 2004, which represents a growth of 26 per cent
- An increasing awareness within the Polish administration that innovation is important for the economic growth and welfare of the citizens.

FRANCE

- The employment in high-tech service and the public R&D expenditures are both increasing.
- An obvious decrease in the private sector is being experienced (reduction of companies' R&D expenditure and employment in medium and high-tech manufacturing activities).
- Relatively bad position in lifelong learning.
- A relevant objective is to increase private research/innovation in enterprises.
- Total R&D expenditure of 2.6% of the GDP, by 2006
- 2005 EIS Summary Innovation Index (SII) Rank: 9

²⁰ *Trendchart; Innovation Policy in Europe*; an initiative of the European Commission, the Enterprise & Industry Directorate General and the Innovation Policy Development unit
<http://trendchart.cordis.lu/scoreboards/scoreboard2005/index.cfm>

THE NETHERLANDS

- The Netherlands aims to raise private R&D expenditure towards the EU average by 2007.
- Public-private relationships and the synergy between education and research could be improved
- Innovation vouchers available for small and medium-sized companies to buy knowledge from public knowledge institutes or large companies with a R&D department.
- The total expenditures on R&D are in a state of stagnation.
- There is a looming shortage of skilled personnel, especially in science and technology.
- Total R&D expenditure of 2.1% of the GDP, by 2006
- 2005 EIS Summary Innovation Index (SII) Rank: 7

SPAIN

- Considering the development of a National Innovation System as a process, the Spanish development of such a system is still at the initial stages.
- The profitability of enterprises, in most cases, is still based on relatively low wages and the reduction of operation costs through purchasing external technology.
- Public expenditure is low.
- The strategy of the European Union is based on reaching a 3% of the GDP invested in R&D by the year 2010.
- Total R&D expenditure of 1.3% of the GDP, by 2006.
- 2005 EIS Summary Innovation Index (SII) Rank: 16

The European Innovation Scoreboard from 2005 confirms Sweden, Finland and Switzerland as the leading innovative countries in Europe.

The following map (figure 7) is provided in order to illustrate the situation of the innovation and its trends within the European countries.



Figure 7: Country groupings in Europe concerning Innovation
Source: the Maastricht Economic Research Institute on Innovation and Technology (MERIT)

3.6 The value chain

The value chain organizes the activities that add value to the company. It is a powerful tool for strategic planning and its ultimate goal is to maximize value creation while minimizing costs.

1. Michael Porter's value chain²¹

In 1985, Michael Porter introduced a value chain model differentiating the activities of the company between the core activities (*primary activities*), and the activities supporting them (*support activities*).

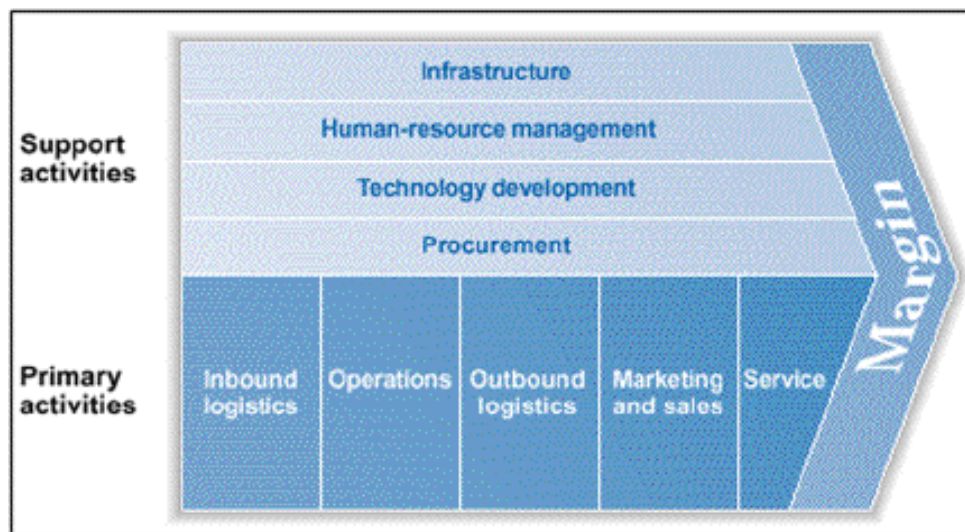


Figure 8: Michael Porter's value chain (1985)

The firm's margin or profit depends on its effectiveness in performing these activities efficiently, so that the amount that the customer is willing to pay for the product exceeds the cost of the activities in the value chain. It is in these activities that a firm has the opportunity to generate a superior value. A competitive advantage may be achieved by reconfiguring the value chain to provide lower cost or better differentiation: innovations may be driven in all the activities of the value chain, not only in research and technology development.

2. Biotechnology industry value chain

The value chain for the biotechnology industry is represented as follows:

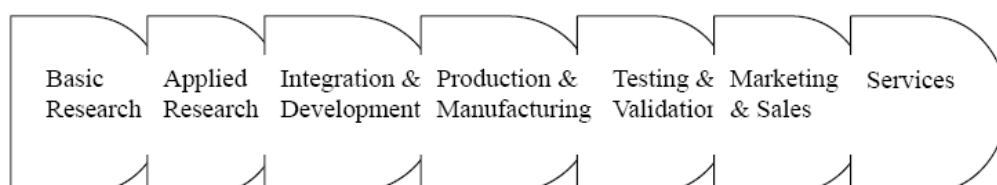


Figure 9: Biotech industry value chain

²¹ Michael Porter; *Competitive Advantage*; 1985.

Before exposing how important is the value chain to understand the biotechnology industry, the main activities integrated in it are described.

- **Basic research**
Basic research is driven by scientists. The main motivation is to expand knowledge, more than to create or invent something. No ambitious commercial value is sought.
- **Applied research**
Applied research is undertaken to solve practical problems, improving the commercial condition of the company. The inventions resulting of applied research are susceptible of being patented.
- **Integration and development**
The main purpose of these activities of the value chain is to define the development process to transform the patented invention into a product ready to be launched into the market.
- **Production and manufacturing**
At this stage of the value chain the company chases the production of the product in large quantities with absolute reliability.
- **Testing and validation**
Testing and validation activities are undertaken to ensure that the properties of the final product are the same as in the applied research stage.
- **Marketing and sales**
The activities at this stage of the value chain seek to ensure the acceptance of the product once in the market.
- **Services**
Services embrace all the activities assumed to support the customer after having acquired the product.

As previously shown within this chapter, biotechnology industry has two main particularities that differentiate it from other industries: its strong influence of science, and a spontaneous division of labour in the research and productive activities. They both are very important to fully understand, not only the value chain, but the biotech industry itself.

Among all the activities, the most relevant are undertaken at the earlier stages of the value chain, which embrace the research and development of new products. Such relevance lies on the fact that most of the resources are invested in these stages. Apart from the resources, the state of the science and knowledge, as well as technology, play as constraints for these activities.

The second characteristic that differentiates biotechnology from other industries is the division of labour between research and productive activities, that is to say, different activities of the value chain are treated separately by the companies. In most cases, companies only focus on some of the activities, as outsourcing subcontractors companies. The concept of outsourcing is developed in the following section.

3. Outsourcing value chain activities

A firm may specialize in one or more value chain activities and outsource the rest. The extent to which a firm performs upstream and downstream activities is described by its degree of vertical integration.

A thorough value chain analysis can illuminate the business system to facilitate outsourcing decisions. To decide which activities to outsource, managers must understand the firm's strengths and weaknesses in each activity, both in terms of cost and ability to differentiate. Managers must consider the following when selecting activities to outsource:

- Whether the activity can be performed cheaper or better by suppliers.
- Whether the activity is one of the firm's core competences from which a cost advantage or product differentiation stems.
- The risk of performing the activity in-house. If the activity relies on fast changing technology or the product is sold in a rapidly changing market, it may be advantageous to outsource the activity in order to maintain flexibility and avoid the risk of investing in specialized assets.
- Whether the outsourcing of an activity can result in business process improvements such as reduced lead time, higher flexibility, reduced inventory, etc.

Outsourcing value chain activities is the way the biotechnology industry works. At this stage of the project it is easily understandable how demanding the biotech industry is. It is not possible for many companies to develop all of the activities; only some huge multinational companies, for example from the pharmaceutical industry, can embrace the whole value chain. But even such firms outsource to smaller companies those activities with a poorer capacity to add value to the process.

In order to be competitive, companies in the biotech industry focus on some of the activities of the value chain, selling the products or components to companies whose activities are located downstream in the global value chain.

This idea leads the project to the next point of the chapter, exposing how the value chain determines the structure and performance of the biotechnology industry. First, a diagram illustrating the main activities that add value to the biotechnology industry and the relationship between them is provided (figure 10):

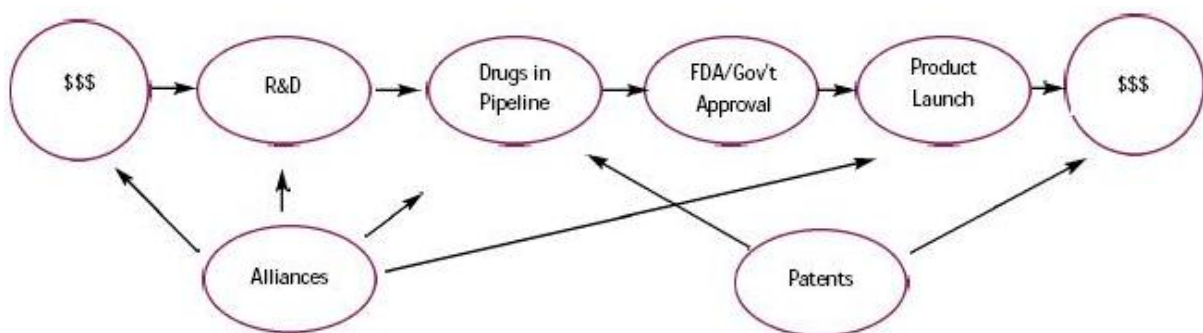


Figure 10: Value creation in Biotechnology

3.7 Biotech industry structure

The biotechnology industry has to be understood as a high-technology industry, as many of the activities within its value chain bear a close relationship to technological processes.

Biotechnology is an industry that demands lots of resources to the companies of the sector. According to company's strengths, it should focus on those most appropriate activities of the global biotech value chain, in order to either enter successfully into the market, or to be competitive once in it.

The same analysis is worthwhile at a country level: a country aiming to enrol on the biotechnology market should first assess its strengths and weaknesses in order to identify those activities within the global biotech value chain on which efficiently focus its efforts, that is to say, identify the profitable niches of the market. Some Asian countries, for example, take advantage of their outstanding knowledge on medical sciences to promote the creation of new companies focused on research activities for medical biotechnology and biopharmaceuticals.

Biotechnology industries can be classified into two main groups, depending on their position on the market, that is to say, depending on the stages of the value chain adopted in the company's activity:

- Core industries:
 - a. Companies that can integrate the entire biotech value chain by themselves. These are multinational pharmaceutical companies with strong R&D capability.
For example: Merck and Pfizer from the US, and Bayer and Roche from Europe.
- Peripheral industries
 - b. Biotech firms that provide pipeline products to the big pharmaceutical companies, with which they form strategic alliances for mutual development. These companies outsource some parts of the process to other firms in order to focus on the product development.
 - c. Firms specialized in certain portion of the development process. They are called *outsource subcontractors*.
 - Contract research organizations, conducting clinical research for biotechnology and pharmaceutical companies.
 - Contract manufacturing organizations, developing research tools and providing chemical substances.

This chained effect existing in the biotechnology market, suggests that the *expansive effect* on biotechnology (including those companies acting as direct and indirect suppliers and customers) is a lot more significant than the *direct effect* itself (from biotechnology companies). It can be said that, on average, each job generated in biotechnology can result in the creation of two further jobs in the purchasing or supplying sectors.

Sources:

- *A methodological approach to the marketing process in the biotechnology-based companies.*; Carla Costa, Margarida Fontes, Manuel V. Heitor; Department of Mechanical Engineering; Center for Innovation, Technology and Policy Research; Instituto Superior Técnico; Lisbon; Portugal; September 2002.
- *Strategic positioning of Taiwan in the Global Biotechnology Value Chain*; Yu-Shan Su; National Taiwan University; International Business Department; Taiwan; 2002.
- Medical biotech value chain: www.soc.edu/NC_GlobalEconomy/biotechnology/

3.8 Management of R&D projects

Since the beginning of the chapter, when introducing biotech products and technologies' life cycles, the particularities of the biotech industry were identified. Then, when talking about the value chain, it was demonstrated how such characteristics determine the structure of the biotech industry and market. This idea is developed in the previous subchapter. At this point, when exposing the management of R&D projects, some characteristics of the biotech industry stand again, determining a particular management of the R&D projects portfolio. As it is developed in next, the methods available for the management of R&D projects of traditional industry cannot be applied to biotech.

3.8.1 Brief history of industrial R&D

At the beginning of the 20th century, companies such as General Electric, and DuPont set their own research laboratories mainly focused on the following lines of research: basic research on new technology areas, and new markets for the company and existing product lines. For the last 20 years industrial R&D has experienced substantial changes. According to them, five generations of R&D can be identified:

- 1st GENERATION: R&D is undertaken without considering the rest of the company's departments, with almost no communication either with them or with the outside. Activities are unpredictable and accidental. R&D finance included within the general costs of the company.
- 2nd GENERATION: during the decade of the 60's and 70's, the R&D departments began to establish links with other departments of the company, breaking its isolation. Matrix structures are adopted. Projects become the core unit of the R&D.
- 3rd GENERATION: until 1980 R&D management is integrated into the company's strategy. Projects portfolio gains importance. Information management becomes great relevance.
- 4th GENERATION: company's R&D is integrated into customer's R&D, in a process of learning together. Customer satisfaction is the main goal. Technological information becomes a competitive arm. The awareness of "productivity paradox": investments in technology do not produce important improvements in productivity. The use of multidisciplinary groups grows.
- 5th GENERATION: company's activities based on knowledge. Innovative activities require the participation of suppliers, customers, distributors and, in general, all agents involved. Company's direction must manage knowledge flow. The main goal is to have the ability to create new ideas and bring them successfully to the market.

3.8.2 R&D strategy led by market or technology

For about 90 years laboratories for industrial research have been working according to an R&D strategy led by technology (*technology push* strategy). Currently, some trends based on focusing R&D strategies on market needs (*market pull* strategy) are imposing.

It is irrelevant to discuss which strategy to follow in order to define and develop R&D projects. From the traditional industry's point of view, there is no difference between both strategies: on the one hand, market needs can only be satisfied once the necessary technology is available. On the other hand, an invention will be worthwhile only if it meets acceptance within the market. From the biotechnology industry's perspective, the reasoning is fairly different. Due to its particularities, above all its strong dependence on science, the ability of a biotech company for innovations is parallel to the improvements in current technologies and knowledge. After all, the biotech products need to meet market acceptance in order to be profitable for the companies.

3.8.3 R&D projects evaluation

In the evaluation and selection of R&D projects, the most determining factor is **uncertainty**. Depending on it, the methods adopted to manage R&D projects portfolio differ notably.

For those projects with a low level of uncertainty, some economic methods may be developed. They are used to assess the profitability of the investment in terms of time and the amount of sales needed to pay them back. Figure 11 illustrates the *discounted cash flow* (DCF) model, a simple model traditionally used to value biotech projects and project portfolios. Through the DCF model, an expected positive future cash flow from the sales and a negative cash flow from the development is discounted. If the net present value (NPV) – the monetary value resulting from subtracting to the initial inversion the cash flow – of the positive cash flow exceeds the NPV of the negative cash flow the project is funded.

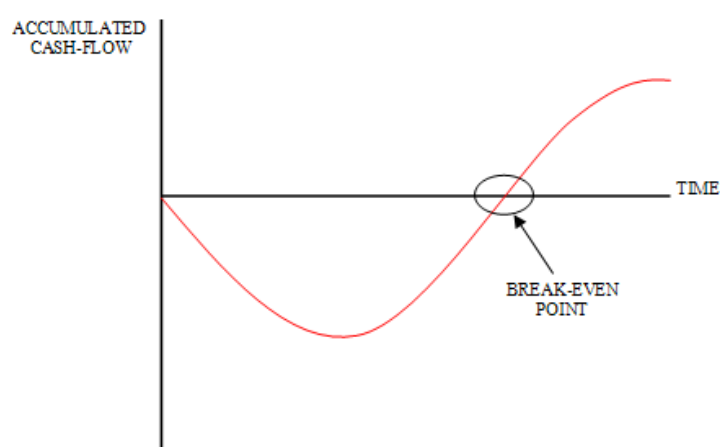


Figure 11: Cash flow accumulated in a project
Source: Twiss, 1974

The *break-even point* of a project provides a measure of the easiness or difficulty to pay off the initial disbursement. It is an important figure to take into account for the selection of the R&D projects within the portfolio.

This approach is too simple and unrealistic, as these economic methods are supported on the predictions for sales and costs of the R&D. For biotechnology and pharmaceutical companies, because of the high level of uncertainty they deal with, the cost of R&D is unforeseeable, therefore, such previsions are impossible to make.

3.8.4 Management of biotechnology R&D projects:

Most of biotech companies rely on venture capital companies and other investors for funding R&D projects. So, it is vital for them to be able to quantify the value of R&D projects – not only for investors, but also for management purposes –. Therefore, biotech companies need a model to calculate both the risks, strategic options and the market uncertainties they face.

As illustrated in the matrix below (figure 12), a *discounted cash flow* approach would be appropriate if there were no uncertainties and a minimum risk. If the situation provided little uncertainty and a number of measurable risks a *decision tree* could be appropriate. But, in the biotech industry the degree of market uncertainty (number of patients, cost of treatment, etc.) is very high, and the degree of risks in the R&D phase (success rates in different stages, etc.) is relatively high. In this situation *Monte Carlo simulation*²² and *real options valuations* are appropriate.

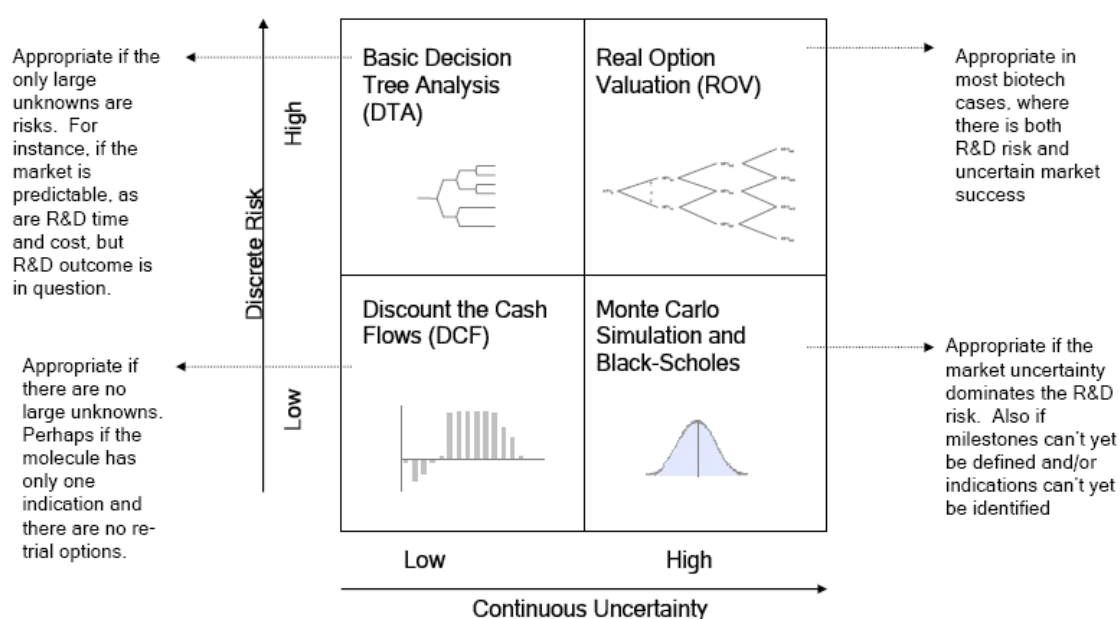


Figure 12: Valuation of biotech projects

Source: *Valuating biotech projects portfolios using crystal ball and real options.*

Aaren Ekelund, Denmark; 2005.

By using Monte Carlo simulation techniques it is possible to quantify market uncertainty in a more tangible and pragmatic way. Market size estimations are made up by a number of parameters for the indications targeted with the R&D projects. Market driver parameters, like the number of patients, the recommended dosage, etc., and cost driver parameters, like cost of goods, sales force need, facilities, etc., for each indication are all uncertain estimates that make up the expected future positive cash flow. Being able to incorporate uncertainty on each of these parameters and then using simulation to quantify these uncertainties provides a more realistic estimation of the future market size and revenues.

Real options techniques enable one to analyze and put value on strategic possibilities and hence the strategic flexibility present in the R&D phase. This means that real options

²² Monte Carlo methods are especially useful in studying systems with a large number of degrees of freedom. They are useful methods for modelling phenomena with significant uncertainty in inputs.

techniques let one give value to strategic options like, for example: abandoning the project if tests fail or expected returns are not lucrative, sell a project, engage in a joint-development agreement to split costs with partners, going to market and establishing own sales forces, etc. Using real options techniques, a value can be assigned to all the strategic options, or one particular strategy can be analyzed given all the uncertainties.

Before ending this subchapter, it should be said that an important part of the value of pharmaceutical R&D projects resides in the *expansion options*: the use of technologies or capacities developed in a project, in other non planned applications in different fields. To illustrate this fact, 60% of pharmaceutical research projects develop drugs that were not initially foreseen (sexual stimulant Viagra was developed as a consequence of research on heart diseases). To evaluate these possibilities *decision trees* are useful.

Source:

Valuating biotech projects portfolios using crystal ball and real options. Aaren Ekelund, Denmark; 2005

3.9 Companies organization for innovation

In research, personal skills and individual characteristics are very important, but they need to be supported by a suitable organizational structure allowing people to develop their aptitudes. This is particularly relevant for companies within an industry such as biotechnology. As a knowledge driven industry, with a tight relationship with science, the level of success of companies depends on how efficiently they manage knowledge. Moreover, the biotechnology industry, as a high-tech industry, requires of the companies, in order to success in the market, to have a structure flexible enough to adapt to continuous technological changes.

On the other hand, the biotechnology industry, as a high-tech industry, requires of the companies, in order to succeed in the market, to have a structure flexible enough to adapt to continuous technological changes.

According to the size of the company, its main activity, the market in which participating, among other parameters, companies adopt one of the following structures:

- Organization for scientific specializations

This structure facilitates the adaptation of the scientists coming directly from universities – it is a suitable organizational structure to train R&D personnel. It is very appropriate to acquire new knowledge on a determined field, but not to solve problems quickly, because it is mainly focused on the long term, and it is set to far from the market and the needs of the operational divisions. Definitely, this a suitable organizational structure for biotech companies devoted to research.

- Organization for projects

Useful when the process to attain a new product consists of some projects, each of them with a defined objective, and coordinated among them. Such structure lies between organization *for scientific specializations* and *matrix organization*.

- Organization for lines of products

It corresponds to a multidivisional organization, in which each division produces a different line of products. Divisions have high autonomy and their own R&D labs. Although this structure is agile and offers a close relationship with the final user, the company may incur in unnecessary duplicities.

- Matrix organization

This model of organization adopts some elements from project management and some others from hierarchical professional structure of the company.

- Direction of risks

Structure adopted for some strategic projects, which are developed independently, creating teams outside the company.

Concluding this subchapter, it is interesting to point out that some biotechnology and pharmaceutical companies mainly focus on the development of long term research programs, perform their activity according to an organizational structure consisting of a parallel secondary line of research and/or manufacturing that develops products requiring short time to be launched into the market, in order to finance the main activity.

Table 2 illustrates the main characteristics of the different organizational structures:

	Organization for specializations	Direction of projects	Organization for lines of products	Matrix organization	Direction of risks
Creation of technological capital	HIGH	MEDIUM	LOW/ MEDIUM	MEDIUM	LOW
Professional development of personnel	HIGH	MEDIUM	LOW/ MEDIUM	MEDIUM	LOW
Formation in management of the personnel	LOW	MEDIUM	MEDIUM	HIGH	VERY HIGH
Achievement of short term project goals	LOW	MEDIUM	MEDIUM/ HIGH	MEDIUM/ HIGH	VERY HIGH
Implication of marketing, production and finance personnel	LOW	LOW	MEDIUM	MEDIUM/ HIGH	HIGH
Technology transfer	HIGH	MEDIUM	LOW/ MEDIUM	MEDIUM	LOW
Identification with the company	LOW	LOW	MEDIUM	MEDIUM	MEDIUM/ HIGH

Table 2: Characteristics of organizational structures
Source: Twiss, 1974

3.10 Cooperation for innovation

Cooperation between companies for innovation

Cooperation may be defined as an agreement between two or more independent companies to share their capacities and resources in order to improve and increase their competitive advantages. Generally, such resources may be of four different types: capital, products technology (patents, designs, results and capacity for research), know-how and commercialization nets.

As it has been demonstrated within the chapter, biotechnology is an industry with a strong influence from science. According to that, the main activities of the value chain, those demanding most of the resources – capital, knowledge and technology – are based on R&D. Therefore, in biotech industries, cooperation agreements between companies are mainly reached on basic research, applied research or technology development.

With regard to the impossibility of companies to embrace the whole biotech value chain within their activities, as the resources needed are overwhelming and only affordable for a few number of multinational biotechnology or pharmaceutical giants, companies in this industry, according to their strengths and weaknesses, focus on those activities that they can undertake efficiently, outsourcing the rest. The value exchanged through these cooperation relationships, as stated above, is mainly based on R&D. Therefore, patents play a key role in it (the importance of patents in biotech industry, together with their definition, characteristics and situation are developed in the last point of the chapter).

Concluding the exposition of the cooperation for innovation, it is important to point out that some biotech and pharmaceutical companies focused on research share their laboratories in order to split the resources to invest in it.

Innovations born outside companies

In the field of innovation we can find many attempts of simplifying or dividing work. Companies search for other companies to outsource some tasks. For many companies the only way of innovation is to cooperate with the university, because they do not have their own R&D department. In the specific brand like biotechnology the obvious thing is cooperation with universities, which have strong base of knowledge, scientists, instrumentation, etc. In this cooperation between companies and universities there seems to be a little dissonance. It is only possible that company will take university seriously, if they protect their knowledge better and systematically (for example by using active policy). On the other hand scientists should have the accountability preserved.

An important role should be played by the Government, fostering knowledge clusters, innovation centres, etc. Because of the fact that developing and introducing new biotech products is enormously expensive, it is very important to realize that the companies, universities and government have to work together during whole process of innovation to reduce the cost and get product at the market faster.

What government can do to make the situation better is changing the infrastructure of the state in a way to assure transfer of knowledge and technology in an easy way. Also changes in educational system should be considered, to make it more flexible.

Institutional support to innovation and R&D

What is clearly visible in the field of innovation and Research and Development is a fact that companies have difficulties in financing their projects. In this problem the support is needed. There are subsidies available from the EU (for example PHARE), regional funds, or governmental refinancing. These funds are very important for many companies, however except if the regulatory issues can also help. Initiatives like tax relief, profitable system of accounts are things that would help companies and in different countries are initiated on different levels.

There also exist institutions that help companies in creating developmental plans, changing infrastructure of the company and many other. All this action is very useful for companies and helps to become more competitive.

International / European technological programs

European Technology Platforms was started in the year 2003 and the main goal of this creation is focusing on strategic issues to achieve Europe's future growth, competitiveness and sustainability in dependence on major technological advances.

The platforms define research and technological development objectives and a way to attain them.

They are a good tool for EU research priorities to unite industry's needs. They cover the whole economic value chain and ensure that knowledge is transformed into technologies and processes.

To achieve goals formulated in the Lisbon Strategy, Europe should specialize more in high-technology areas, invest more in researches. Using Platforms is a good solution to reach this goal because they have positive impact on a wide range of policies, reduce fragmentation of research and development efforts and mobilize public and private funding sources.

3.11 Patents

Patents are a tool to grant the exclusivity of exploitation of an invention to the person or company responsible for it, in order to compensate the effort invested in it. Without such protection, no company would spend the copious amounts of resources needed to develop an innovation, knowing that it can be copied by competitors. Patents provide a protection of the invention for 20 years. Afterwards, the invention is considered public domain.

More than 4 million patents are recorded around the world and, each year 800.000 demands are made.

The patents need to meet the following basic requirements in order to be issued:

- The invention must be new world-wide, not integrated with the current state of technical knowledge.
- It must result from inventive activity, that is to say, supported by an intellectual process.
- It must be susceptible to industrial application.

It is important to remark that discoveries of products or organisms existing in nature are not patentable. Some other exceptions to patentability are:

- Creations belonging to public domain. For example, scientific discoveries.
- Inventions protected by intellectual property, such as scientific theories, mathematical methods, artistic and literary work, and computer software.
- Not protected inventions: inventions against moral and public order, animal breeds, and procedures, essentially biological²³, of obtaining vegetables and animals (however, microbiological procedures and the products obtained through them are patentable).

As it was discussed in the first chapter, when introducing the ethical problems concerning biotechnology, patents also face a moral or ethical debate when the patentability of human cloning processes and genetic manipulations, and the use of embryos for industrial or commercial purposes are discussed.

The European Ethical Group on Science and New Technologies proposed to patent biotech inventions in 1993, biotech inventions concerning humans in 1996, and human stem cells in 2002. On the other hand, the Japanese office of patents is allowed to patent parts of the human body, as genes and proteins. The same happens for the use of stem cells with therapeutic purpose and for the process of primate cloning, except human beings – a law banning it was adopted in 2001 –.

Once a general idea about patents has been provided, the chapter will focus on the requirements and main characteristics of the patents in the biotechnology industry.

²³ Microbiology refers to microscopic and ultramicroscopic organisms, whereas biology studies vital phenomena of cells, individuals and reproduction.

Patentability of biotechnological inventions:

Patents are a relevant part of the biotechnology market, since the business for the biotech companies focusing their activity on research is selling patents. This is the way that outsources subcontractors work.

Although a discovery of something existing in nature is not patentable, a natural product isolated and purified is patentable, as it is considered that an inventive activity is needed to invent it. Thus, DNA and biological material, in their isolated form are patentable. Furthermore, the industrial application, together with the invention and the inventive activity, is an unavoidable requirement for patentability. As an example, a human gene cannot be patented, but the process in which the gene will be used (to develop a drug or a treatment, for example) can.

With regard to the patentability of biotechnological inventions, on the 18th of May 1998, the European Parliament considered the proposal formulated by the European Commission, mainly containing the following points:

- Biological material is, in general, patentable, although it exists in nature, if its industrial application is clearly specified in its solicitude.
- Some procedures and methods excluded are:
 - Procedures of human reproduction through cloning.
 - Procedures for the modification of the genetic identity of human beings.
 - Methods using human embryos.
 - Processes for the modification of genetic identity of animals that may cause them suffering, with no relevant medical benefit for humans or animals, and also animals resulting of these processes.

Researchers differentiate reproductive cloning of human beings (completely forbidden world-wide) and human cells cloning for therapeutic reasons (some countries are starting to consider modifying their legislations to accommodate such techniques).

Concluding with the patentability of biotech inventions, it is important to remark that the profitable life of a biotech patent is shorter than 10 years, as the process since the patent is issued (invention) until the launch of the product into the market takes around 10 years.

The different ways that inventors and companies have to apply for a patent are the national path, the European and the international, depending on the potential market of the invention.

National way :

Every state has its own regulations and procedures to concede patents.

If it is desired to introduce the patent into other countries, as many forms as countries need to be filled in. In those countries where the patent has not been solicited, the information is regarded as public domain and the invention can be exploited openly.

In 1883, an agreement was signed by which many of the industrialized countries provide the person or company soliciting a patent in one of the countries with a period of a year to solicit the patent in other countries within the signing ones.

It states two main benefits:

- Soliciting the patents in the different countries at the same time presents severe difficulties and high costs.
- Being provided with a lapse of time permits the company to decide in which countries to solicit the patent.

The national offices of patents for the European countries within the scope of the project are:

- The Offices of Patents of the Republic of Poland, in Poland.
- The Bureau for Intellectual Property, in the Netherlands.
- The National Institute of Industrial Property, in France.
- The Spanish Patent and Trademark Office, in Spain.

European way:

In 1973, was signed the Munich Convention about European patents, called CPE path. The signing countries were: Germany, Austria, Belgium, Cyprus, Denmark, Spain, Finland, France, Greece, Ireland, Italy, Liechtenstein, Luxemburg, Monaco, The Netherlands, Portugal, United Kingdom, Sweden and Switzerland.

The convention states that a common agreement to concede the patent in these countries with only delivering a single solicitude, in a single language (English, French or German), and obtaining the protection of the innovation in all those countries designated in the solicitude.

The European Office of Patents (OPE) submits the request to an examination of novelty and inventive activity. Only the 60% of the requests are conceded.

The cost of patenting an invention in a European scale proves to be more economical, when the number of countries chosen is higher than five, otherwise it is better to request the patents country by country.

Community patent: concession of patents valid across all the countries of the EU, with the associated safe of costs and simplification of the process.

Concluding this section, the figure below (figure 13) illustrates the precedence of the demands of patents to the EPO.

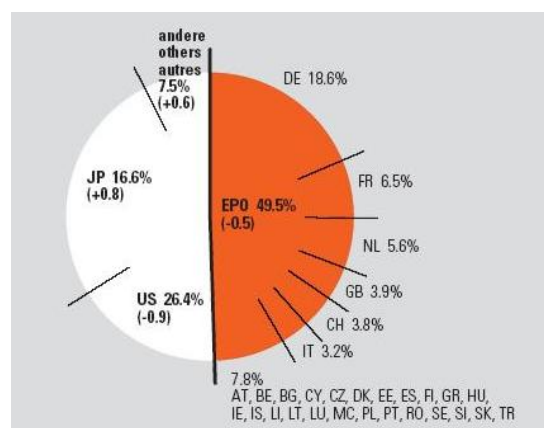


Figure 13: Origins of the EPO patent demand

International way:

In 1970, the PCT cooperation treaty on patent matters was signed in Washington. The PCT is only an administrative vehicle to register patents' solicitudes. Furthermore, PCT cannot concede or refuse solicitudes, as such competences are held by the national offices. The process starts soliciting the patent to the WIPO (World Intellectual Property Organization), set in Geneva. Then, this institution channels it through the national or the European path.

The institution responsible for patents in the US is the United States Patent and Trademark Office (USPTO), in China is the State Intellectual Property Office (SIPO) and in Africa is the African Intellectual Property Organization (OAPI).

To be aware of how many biotechnology patents are issued, it should be pointed out that from 1987 to 1997, 16,246 biotech patents have been registered in Europe by the EPO (8,468 from the US, 5,742 from Europe and 2,036 for Japan). In the United States, USPTO states that from 1987 to 1993, 16,656 patents were filed from the US, 5,052 from Europe and 3,366 from Asia. The superiority of the United States with regard to the number of patents issued began in 1990, and from then on the gap between Europe has been increasing. Since 1999, China has become a global competitor, with a number of applications for patents in 2000 – most of them from the inside of China – bigger than the demand in Japan or in Europe.

To sum up, the biotech sector experiences quite a dynamic trend, as USPTO and EPO registered a rise of between 10% and 15% in the number of biotech patents issued, whereas the increasing rate for the rest of the patents is only of 5%.

Source:.

Rapport sur la place des biotechnologies en France et en Europe from the Office parlementaire d'évaluation des choix scientifiques et technologiques

Main source of chapter 3:

Tecnología e innovación en la empresa. Pere Escorsa, Jaume Valls. Edicions UPC. 2003

Chapter 4

Empirical verification

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Introduction

In the first three chapters the concepts of biotechnology and innovation, together with their most relevant characteristics, particularities and situation, have been presented. The aim of this part of the project is to present a real biotech company functioning in Poland and to contrast the general contents exposed in the previous chapters with the information obtained from the company's analysis.

4.1 The company: BTL Sp. Z o.o.

The biotech company analysed is BTL, a small Polish firm that focuses its activity on the production of bio-products (peptides, indicators, extracts from meat and plants and pepsin – both for veterinary tests and pharmaceutical products manufacturing), consulting services and distribution of indicators and other laboratory accessories.

BTL was set up after the privatization in 1990 of a state-owned company whose core activity was based on meat wastes utilisation. At that time, BTL was set as a limited liability company. It took over the buildings, existing for over 40 years, machinery and all the technology. Its main activity was focused on the production of enzymes and microbiological bases, used to identify bacteria in food – cheese and meat, for example – and in the facilities where it is processed.

Today the firm counts twenty employees (not including the ten employees of outsource subcontractors of certain activities, such as cleaning, reception, etc.) and has a turnover of above 2.000.000 PLN (about 500.000 euros). Its sales team estimates to have between 7 and 10% of Polish market share of all microbiological bases (traditional powder form, liquid form and the ready-to-use bases, which is produced in Poland only by BTL). Most of its about 2000 clients – laboratories of milk producers, sanitary and epidemiologic institutions, veterinary inspection, water and canalization inspection, pharmaceutical industry, universities and everywhere where the microbiology of products is analyzed – are small and medium sized enterprises, although there are also a few large intuitions (public as well as private). Last year, the client base contained over 1500 records, having grown 500 points this year, which shows that the company is developing. BTL bases its production on demand, so it does not have important stocks. Its products are promoted at trade fairs and scientific symposia and advertised in specialized magazines (for example, *Laboratorium*).

Proving the eagerness of BTL for surpassing the customer's expectations, processes of creating, manufacturing and production are granted by the ISO 2001:9000. With regard to it, the firm opted for the prestigious German audit company TÜV, willing to be comparable with other companies – mostly very large – in the industry; TÜV is the audit company for both MERCK and Biomerieux, two large multinational firms competing with BTL. Every so often BTL conducts internal audits, additionally to the official external inspections driven once year by auditors from TÜV. It is important to remark that, although BTL is selling its products only in Poland, many of its direct clients sell beyond Polish borders, which means that producing according to international standards is a must. Moreover, BTL was awarded in the year 2000 the Fair Play title, showing they are friendly to customers, employees and the environment, as well as correctly fulfilling their obligation towards the social security and tax offices. In the same year a hygiene program was implanted concerning safety during the processes of production, warehousing and packaging. According to it, the facilities are divided into three zones: the *black zone* (the least hygienic area, like offices and corridors), the *grey zone* (a more hygienic zone where clothes and shoes protection is needed. Such a zone contains part of the production and physical laboratories) and the *grey controlled zone* (the most hygienic zone, which can be entered through special gates – sluice gates – and requires changing clothing and footwear. In this zone, most of the production and packaging is made).

Once the firm has been introduced, the exposition will focus on how the company's strategy and performance adopt most of the ideas developed through "Managing innovations in biotechnology" previous chapters.

4.2 Innovation

BTL clearly understands how important innovation is to be competitive on the market, and therefore it is putting considerable efforts in innovation, through the development of new products to match customer expectations. Most of its clients are small and medium sized enterprises which do not have adequate resources for the development of the products needed in their processes. Responding to these needs BTL develops ready-to-use products, which do not demand specialist equipment – not affordable for such companies. A new product of BTL, consisting of microbiological bases on plastic plates, illustrates this idea.

The innovative process

At the beginning of its activity the firm produced microbiological bases in powder form, which required the final user to measure the proper amount precisely (measurement equipment necessary), next to add distilled water of a certain temperature and incubate the substance in an autoclave – a pressurized device designed to heat aqueous solutions above their boiling point, which is a costly equipment, worth of around 60.000 PLN (15,000 euros) – in order to receive a gel ready to be used to check the cleanliness of the products or equipment. In order to assist customers in the improvement of their processes, BTL developed through research (applied research, according to what is exposed in the part of the chapter 3 presenting the innovative process) a product ready to use, that required no additional equipment from the customer. No other Polish company managed to do so. Even though competitors in Gdansk and Warsaw tried it, they did not succeed in obtaining the correct characteristics of the gel – instead of a convex meniscus sticking out from the plastic case, necessary for the product to be applicable, competitors obtained concave meniscus that were useless for the final user. So, BTL is the only Polish company producing such microbiological bases on plastic plates that are ready to use for the customer. Because of its exclusivity of production in Poland, the only fear of BTL arises from foreign competitors. Although, the characteristics of the product play in favour of the firm, as the product perishes within a short time – between two and three months – and the conditions for transportation are strict – it must be kept in the dark and in a proper temperature, not too low and maximum 25°C .

Its innovative microbiological base is tested in BTL with Polish and ATCC (USA) cultures²⁴. ATCC cultures are used in Europe and in the rest of the world as standards of testing microbiological products. Although the use of other cultures is possible, it does not grant that the result of the testing is trustable. Therefore, both direct and final customers require the utilization of ATCC cultures.

²⁴ Populations of microorganisms.

Product life cycle

The demand for the new product is growing at a very high pace. At the early stage, in 2005, between 100 and 300 bases produced in a laboratory fashion were sold monthly during a few months. Now the product has reached its growing stage with sales up to 6000-7000 units per month. This enormous success of the new product is not only due to the fact that it exactly fits client requirements at a cost lower than traditional bases (in terms of necessary equipment) but also to the fact that the sanitary requirements that have to be met by BTL's clients have increased the number of tests to be done.

Currently, BTL is working on a new product, consisting of microbiological base in a test tube which can be sold to small enterprises and laboratories that test liquid substances. As the microbiological bases in a plastic plate, developed before by the company, such product would enable the final clients to reduce costs of testing and to simplify the testing process. This is another example of innovation through applied research, undertaken by the company.

Types of innovation

As shown in chapter 3, when developing the innovative process, it is remarked that reducing innovation to research is not accurate. Obviously, for biotechnology companies such as BTL, the connection between R&D and innovation is much more outstanding than in other industries, but the concept of innovation is yet more complex. Back to the analysis of BTL, this situation is illustrated by the fact that the company, as a conclusive proof of its commitment to improve its activity through innovation, is building a new laboratory for the production of microbiological bases and incorporating new equipment to automate their production.

The value chain

With regard to the BTL value chain, according to what is shown in the project about the biotech global value chain, its main innovations are mainly focused on two stages: applied research – with the development of the microbiological bases through R&D – and manufacturing and production – with the improvement of its facilities and equipment. Furthermore, in developing new products BTL tries to assume the ideas used by its larger (often foreign) competitors, of course respecting the knowledge protection regulations that might be involved.

As a conclusion of the two previous paragraphs, it can be stated that BTL is supporting its activity on the innovation. At the same time, their innovative strategy is mainly focused on R&D and production.

4.3 Organizational structure for innovation

As developed in chapter 3, innovative companies need to have an organizational structure allowing them to efficiently turn their ideas into successful products. BTL does not strictly follow any of the structures introduced previously. BTL has about 20 employees, virtually all of them with diploma of higher university degrees. Most of the employees work in the laboratory, in the production department and are also responsible for selling and client contacts – customers expect to deal with competent experts on products. This particular organizational structure provides BTL with an important level of flexibility, as all the employees have a comprehensive knowledge of the industry (market needs and characteristics of the products, processes, technologies, etc.). However, it is important to remark that, as far as the company grows, this strategy may become poor.

4.4 Cooperation between companies for innovation

An important point of the biotechnology industry, as stated in the project, is the cooperation between companies and institutions for innovation. For a long time ago BTL has maintained a cooperative relationship with the Technical University of Lodz (TUL). However, due to lack of funds from external sources their research remains on a basic level, as higher research involves very high costs, not affordable either for the company or the university. As an example of a cooperation project between BTL and the TUL: they tried to develop quick test indicators to be used in the milk processing industry, which would accelerate the verification of the quality of the product. Because of the scarcity of funds, the project had to be rejected.

4.5 Financing between companies for innovation

Another relevant point to be considered when thinking of the biotechnology industry is obtaining external funds. When talking about the institutional support to innovation and R&D, it was said that some national governments subsidize those companies that invest on innovation or on R&D. Additionally, the European Union has also a budget with this purpose. It is important to remark that, as stated in the analysis of the situation of innovation in the EU, the strategy for developing innovation in Poland, mainly focused on the development of R&D, comes from the private sector. Supporting that, BTL does not obtain external funds and therefore it only operates and conducts research from its own capital. Even when grants from EU funds were deposited, formal mistakes in the complex bureaucratic system disqualified the projects. One of the possibilities to be assessed by the firm is the assistance from an external expert to conduct the application process, but this is costly for such a small company. It is important to remark that Polish government spends little money on promoting R&D and innovation.

4.6 Patents

The analysis concludes with the protection of the inventions. According to what is developed in the subchapter dedicated to patents, their role in the biotechnology industry is extremely relevant: as a knowledge-driven industry, supported on research, there are lots of inventions, which suppose important investments of resources – capital, knowledge and technology – that can be easily copied by the competitors. So, unless the inventions can be protected, no company will make such an effort. Back to the analysis of the firm, the company acquired by BTL had a patent on the production of peptines, in the late 70s and early 80s. Then, a patent for Aminobak (a chemical substance) was obtained. Both of them have since then expired. Although BTL is aware of the fact that patents are very important for the protection of the ideas that are developed in their laboratories, the costs to be assumed and the difficulties to face are unaffordable for BTL. After all, there is also a reason for which patent protection is not something that the company cannot function without, because many biotechnological inventions do not need to be copied by competitors as they may reach similar results through a different technology.

Conclusions

The last twenty years took the biotech sector an enormous run. The main reason for this run is an increasing demand for a durable life which results in the improving of plants, industrial production processes and healthcare. With the results in the last twenty years the expectation of biotechnology for the next twenty years is very high and, for example, the percentage of biotechnology in pharmacy will increase to one of the most important sources of new medicines. Curious is the current discord in biotechnology worldwide. The United States is the leading country in the world with a global turnover of 78% and Europe is a marginal player in this field. But since the year 2000 when the Lisbon Agenda was formulated and signed there have been indications that the European biotech and especially the development of new products in biotech will increase. But according to the Lisbon Agenda and the measure of conservatism in case of ethical issues there are big differences in how every European government supports their own innovative (biotechnology) programs through companies and institutions. Also there is a difference in the will for non-biotech related companies to invest in innovative companies in the European countries. The current trends in biotechnology innovations are mentioned below.

Main trends in biotechnology innovations

These concluding trends are based on the characteristics and trends in biotechnology in the four described countries and the results of the European Innovation Scoreboard 2005 (EIS).

POLAND

In Poland there is a potential for R&D in biotechnology but only if the private and the public sector is working together. The public system is already available, with 21 high level universities, but the government must consider a substantial budget for multidiscipline innovation projects (public combined with private) and simplify the bureaucratic system and high tax tariffs.

FRANCE

France can maintain its high position in biotech in Europe but only with investments into the private companies for developing new projects into business R&D departments. At the moment the French government supports (new) innovative biotech company's through very low taxes, another 'public support tool' is not possible because France has a protocol that says that it is not allowed to support private projects. The future for France biotech is dependent on lots of money for innovative R&D, and probably a low tax rate is not enough, seeing that the financing through venture capitalists in other countries is much higher. But there are also opportunities:

To develop the private projects they need employment and in the last years the employment in the public institutions has been increasing. So there a win/win situation can be created; the public sector can cooperate with the private sector to set up new projects or complete new business R&D's and an obvious result of this can be that part of 'public workers' changed their job to a private company.

THE NETHERLANDS

For around five years the research and development in biotechnology has been experiencing a strong pace in the Netherlands. That explains also the ranking of the innovation index²⁵; the 7th place. The biotechnology is not a big sector in the Netherlands; countries like Belgium or Slovenia have a bigger percentage of biotechnology firms in the GDP than the Netherlands. It is conspicuous that the Dutch biotech sector is the opposite of Spain; this country has a huge biotech industry but is very weak in innovation. The main reason of the high ranking in innovation is attributed to the investments by venture capitalists made in the last five years. The results of these investments are not established; some of the biotech companies have huge turnovers but till now they have never made any profit.

There are more weaknesses in the Dutch biotech sector; there is a looming shortage of skilled personnel, especially in science and technology and also public-private relationships and the synergy between education and research could be improved because at the moment they are working like two islands with only a small bridge.

SPAIN

Spain is a country which has a good position concerning contribution to the world scientific production relating to biotechnology; a higher rank than that of, for example, Italy or the Netherlands. Spanish low position in the European innovation rank is very noticeable. This can be explained: the profitability of enterprises, in most cases, is still based on relatively low wages and the reduction of operation costs due to the purchase of external technology. Obviously when the enterprises purchase the technology in other countries; it is not very useful for the development of Spanish innovations.

The result is that there is no climate to invest in R&D/innovations because the zest is low and that is obvious because there is not any perspective in the following 10 years in investing in high-technology.

Recommendations

Through the globalisation of the world and the fast-growing level in R&D in some Asian countries it is necessary for the European Union to set up some protocols or regulations to make their members be aware of the importance of new innovations in biotechnology. Some of these measures could be:

- Oblige every EU member to reserve a minimal percentage of their budget for innovative programs. Probably because of the growing importance of biotechnology in innovations, a substantial part of this money will go to innovations in biotech.
- Support private investments in biotechnology by means of tax benefits during the start-up phase of the development process.
- Set up one clear European protocol to obtain subsidies from the national government; in the current situation each country is completely different and in most of the countries too bureaucratic, especially in Poland. When this protocol is implemented it will support and motivate new innovative ideas with great economical prospects in the future.
- Better patent protection of new inventions. In the current situation it is too expensive and complicated to request a patent for an innovative product or process. This is a good task for the European Office of Patents to make an overview of the main problems in every state, analyze them together with the problems in the other EU members and implement a consistent solution to all of them.

²⁵ *Trendchart; Innovation Policy in Europe*; an initiative of the European Commission, the Enterprise & Industry Directorate General and the Innovation Policy Development unit

Annex

The Lisbon Agenda

The Lisbon Agenda is a plan formulated in March 2000 by the European Commission, in Lisbon (Portugal), by which is intended for Europe to become the world's most competitive economy by 2010.

The Lisbon Agenda settled an overall strategy for the European Union aimed at promoting economic growth, fostering competitiveness and job creation, and advancing structural and regulatory reform, while ensuring social cohesion and environmental sustainability.

The European Union has set a target that overall spending on innovation and research and development should be increased to 3 percent of GDP by 2010, with two thirds of this spend coming from industry.

The Lisbon Agenda has been designed under the belief that the economy for the 21st century will be knowledge-based. According to the opinion of some of the Lisbon Agenda architects, by 2020 Europe will be the world's top knowledge economy²⁶. Furthermore, from the European Commission point of view, life sciences and biotechnology will have a relevant role in this knowledge-based economy.

With regard to biotechnology, the European Commission states that the biotech strategies in the EU countries need to be updated, tuning it to the Lisbon Agenda before 2007²⁷.

Source:

UK Presidency of the European Union 2005; the Lisbon Agenda.

²⁶ *Biotech science thriving but the business needs intensive care*, February 2005; Professor Joice Tait (Director of Innogen Center); www.innogen.ac.uk/conference/

²⁷ EurActive News, October 2004

